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Doctor's Dissertation

Reaction Products of Lignin Model Compounds and Sodium Hydrosulfide

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A STUDY OF THE REACTION PRODUCTS OF LIGNIN MODEL COMPOUNDS AND SODIUM HYDROSULFIDE

A thesis submitted by

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INTRODUCTION

Although the kraft process has been in use for many years, there is no sound explanation of the role played by the sulfide ion in the cook. The mechanism of the delignification of wood in the cook is little understood. One reason for this lack of understanding is undoubtedly the complexity of lignin.

In recent years, considerable attention has been directed toward the use of model compounds in studying the structure and reactions of lignin. The advantage of using model compounds lies in the fact that a known substance replaces a complicated or unknown material in reaction studies. The value of such studies depends largely upon the degree of resemblance of the model substance to the material it represents. Unfortunately, investigations with model compounds are indirect studies, and one must therefore be cautious in drawing positive analogies between reactions of models and reactions of lignin.

An intelligent choice of lignin model compounds requires a partial understanding of the structure of lignin. If the reactions of the model compounds are to be interpreted in the light of lignin reactions in the kraft cook, then the investigations of thiolignin must be considered. Finally, a brief review of the previous studies with lignin model compounds would be desirable.

HISTORICAL REVIEW

The structure of lignin is still unknown, even though innumerable investigations have been aimed at its elucidation during the past hundred years. The failure of investigators to isolate a uniform lignin sample, identical with the original or protolignin, has been a great hindrance. Isolated lignin is an amorphous polymer that varies in composition and complexity, depending upon the source or the techniques employed during its isolation. Brauns' isolated native lignin (1), although obtained in relatively small yields compared with the lignin content of wood, is probably the only lignin sample relatively unchanged during its isolation.

The many investigations of lignin have not been fruitless. Indeed, there are many pertinent facts about the constitution of lignin that have been agreed upon by lignin chemists. Brauns (2) has presented a discussion of the "proven chemistry of lignin". A summary of the pertinent facts includes:

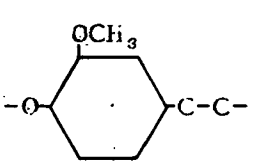
(a) Lignin consists of benzene nuclei, of which the main portion contains three-carbon side chains and methoxyl groups. Degradation products of coniferous lignin are of a guaiacyl type and include vanillin and acetovanillone.

(b) Isolated native lignin, although not proven identical with protolignin, may be a reasonable facsimile. According to Brauns, the spruce native lignin building unit (molecular weight of 840) contains

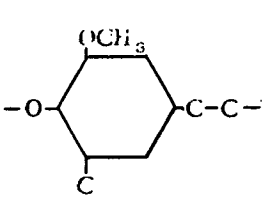
four methoxyl groups, three aliphatic hydroxyl groups, one phenolic hydroxyl group, and one enolizable carbonyl group.

The types of linkages which exist between building stones in the lignin polymer is still an open question. Ether linkages between the phenolic hydroxyl group of one building stone and a carbon side chain of another building stone are possible. There is also evidence for the carbon-carbon linkage between lignin building stones. Isohemipinic acid was obtained by a mild alkali treatment of methylated lignin, followed by methylation and oxidation (3, 4). The formation of isohemipinic acid indicates that some of the benzene rings in lignin contain carbon side chains at the 1- and 5-positions.

Leopold (5) has presented a summary of the results obtained from a comprehensive program of research designed to investigate the technical and economical possibilities of adapting the alkaline nitrobenzene oxidation of lignin raw material to the commercial production of vanillin. The studies have led to the conclusion that lignin is built up of equal numbers of C_6-C_3 units of types I and II connected by ether and carbon-carbon linkages. The



I



II

investigations were mainly studies of vanillin yields or of the yields of products containing only one C-aryl bond, from oxidations in alkaline media

of various model substances and of sprucewood. There was strong evidence for the occurrence of reactive groups at the α-positions of at least one third of the lignin building stones.

The reactions of lignin during the kraft cook are unknown. The lignin products from the kraft cook, the thiolignins, are not simple compounds, but are polymers similar to other isolated lignin samples, except that sulfur is chemically combined. Ahlm (6) investigated spruce thiolignin (3-4% sulfur), using the same techniques employed by Brauns (1) in the study of native lignin. The techniques included methylation with diazomethane, dimethyl sulfate, and methyl alcohol and hydrochloric acid. Ahlm also obtained an acetylated derivative and a mercuric salt from thiolignin. On the assumption that thiolignin is a derivative of Brauns' native lignin (i.e., thiolignin is formed by a substitution or addition reaction of sodium hydrosulfide and native lignin), Ahlm concluded that the thiolignin building unit (molecular weight 857) contains four methoxyl groups, three aliphatic hydroxyl groups, one phenolic hydroxyl group, and a carbonyl group consisting of an enolic hydroxyl and a thiol group. The methoxyl content of thiolignin obtained from a prolonged cook was found to be lowered, but the decrease was too slight to explain the mechanism of the introduction of sulfur into the lignin molecule.

$$C_{41}H_{31}O_6(OCH_3)_4(OH)_3(OH)C(OH)SH$$

Ahlm's Thiolignin

Merewether and Lahey (7) have studied the thiolignin obtained from the commercial pulping of the eucalypts. The techniques employed were

methylation with diazomethane, methylation with dimethyl sulfate, acetylation, and reactions with phenylhydrazine and p-nitrophenylhydrazine. A molecular weight of the lignin building unit of 1324 was obtained by potentiometric titrations and by the Rast method for hexamethyl derivatives. Merewether's investigation (7a) indicated that a thiolignin building unit contains no primary hydroxyl groups, three secondary hydroxyl groups, one carbonyl group, one phenolic hydroxyl group, and a thiol group. The formation of an osazone indicated the presence of a hydroxyl group adjacent to a carbonyl group.

$$C_{52}H_{35}O_{10}(OCH_3)_9C(CH_3)(OH)(CHOH)_2(CH_2 \cdot CO \cdot CHOH)(OH)SH$$

Merewether's Thiolignin

Brauns and Buchanan (8) prepared thiolignin by the action of sodium sulfide on hydrochloric acid spruce lignin. They concluded that one sulfur atom enters each lignin building unit (molecular weight of 840).

One of the first investigations of lignin with model compounds was carried out by Holmberg (9). He showed that methylphenylcarbinol reacts with bisulfite under the conditions of the technical sulfite cook. This alcohol resembles lignin, not only in regard to sulfonation but also in reactions with thioglycolic acid (10) and ethanolic hydrochloric acid (11). Holmberg considered that a hydroxyl group activated by a benzene ring in the alpha-position is of great importance, not only in the reactions of lignin mentioned but also in the condensation reactions of lignin. A series of lignin model compounds, containing the α-hydroxyl group, were

prepared and studied by Lindgren (12). His results supported Holmberg's contention in that the sulfonation reactions proceed almost quantitatively with an activated α-hydroxyl group. The guaiacyl type of substitution causes even more activity.

Wacek and Kratzl (13) considered various model compound reactions with respect to the sulfonation of lignin and the subsequent formation of vanillin. Particular attention was directed to compounds containing a conjugated double bond--e.g., α, β-unsaturated ketones. Wacek and Kratzl claimed that the α, β-unsaturated ketone grouping was masked in lignin prior to the reaction with bisulfite. Sen (14) also studied the sulfonation of different α, β-unsaturated ketones and model compounds containing heterocyclic oxygen rings.

Relatively little use has been made of model compounds in the study of lignin reactions during the kraft cook. In view of Hägglund's work (15) on the delignification of wood by pulping with a buffered hydrogen sulfide solution at 100°C. (pH 7), Enkvist (16) studied the reactions of various model compounds using the same cooking conditions. These model compounds included eugenol, isoeugenol, veratrole, acetovanillone, vanillin, and vanillyl alcohol. Enkvist found that only vanillyl alcohol reacted significantly; in this case, a 50% yield of vanillyl disulfide was obtained. He concluded that the hydroxyl groups of lignin are responsible for the formation of thiolignin. Enkvist also cooked vanillin and vanillyl alcohol with a sodium hydrosulfide liquor (pH 8.1) at 160° for five hours. Approximately 15% of vanillin was recovered from the

vanillin cook, in addition to unidentified amorphous materials containing sulfur. The vanillyl alcohol cook yielded 10% of vanillin and other unidentified material. The formation of vanillin in the vanillyl alcohol cook was explained by an alkaline decomposition reaction of vanillyl disulfide. Enkvist recovered 45% of vanillin when vanillyl disulfide was refluxed with dilute alkali. He suggested that vanillyl disulfide was formed at 160° from vanillyl alcohol but was, in turn, decomposed to form vanillin, hydrogen sulfide, and possibly vanillyl mercaptan.

PRESENTATION OF THE PROBLEM

During the kraft cook, one of the reactions taking place involves the chemical binding of sulfur to the lignin molecule. The introduction of sulfur may take place via one or several reactions. Various intermediate sulfur compounds may be formed prior to the sulfur compounds that finally exist in thiolignin. The types of sulfur linkages actually existing in thiolignin have not been definitely established, and the chemical reactivities of different functional groups with the alkaline sulfide ion have received little consideration. Such is the picture facing the investigator of lignin reactions in the kraft cook.

The purpose of this investigation is to gain information concerning the reactivities of different functional groups with the alkaline sulfide ion. An examination of previous lignin investigations indicates that four types of functional groups are of particular interest. These are the aliphatic hydroxyl group, the carbonyl group, the ether linkage, and the "masked" conjugated double bond similar to that suggested by Wacek and Kratzl (13); based on these groupings, four mechanisms for the introduction of sulfur into the lignin molecule can be postulated by their reactions with sodium hydrosulfide.

(a.) A hydroxyl group may react by splitting out water.

$$ROH + NaSH \longrightarrow RSNa + H_2O$$

(b.) A carbonyl group may react to form a hydrated thione.

$$R_2CO + NaSH \longrightarrow R_2C(OH)SNa$$

(c.) Ether linkages may be split with the introduction of sulfur.

$$ROR + NaSH \longrightarrow ROH + RSNa$$

(d.) Masked conjugated double bonds may be liberated and react.

$$-COCH = CH- + NaSH \longrightarrow -COCH_2CHSNa-$$

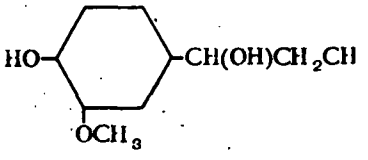
Thus, the problem involved the selection and synthesis of different lignin model compounds containing the desired functional groupings. The compounds were subjected to the action of the alkaline sulfide ion under conditions similar to those of the kraft cook. The products were isolated and identified and, when possible, the course of the reaction was described. Special attention was directed toward those model compounds which combined with sulfur.

EXPERIMENTAL PROCEDURES

SYNTHESIS OF COMPOUNDS

All temperatures are in degrees Centigrade. Melting points were determined in a capillary and are uncorrected.

SYNTHESIS OF 1-(4-HYDROXY-3-METHOXYPHENYL)-1-PROPANOL (I)



(I)

1-(4-Hydroxy-3-methoxyphenyl)-1-propanol was prepared by the method of Roberti, York, and MacGregor (17).

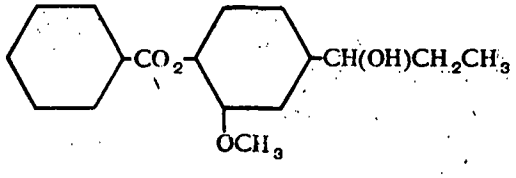
Magnesium turnings (38 grams) and 300 ml. of anhydrous ether were added to a three-necked flask equipped with a condenser, stirrer, and dropping funnel. Ethyl bromide (170 grams) was dissolved in 300 ml. of ether, and 25 ml. of this solution were added to the contents of the flask. (The reaction began after adding an iodine crystal and rubbing the magnesium with a stirring rod.) The remaining ethyl bromide solution was added slowly after the reaction had commenced. The reaction mixture was stirred for 30 minutes after all the ethyl bromide had been added.

Vanillin (40 grams) was dissolved in 800 ml. of ether and the solution was added to the Grignard reagent during a 1.5-hour period. The mixture was stirred for an additional hour and was allowed to stand overnight. Saturated ammonium chloride solution was added to hydrolyze the Grignard complex. The

procedure of Roberti, et al. indicated that the ammonium chloride was sufficient to bring about hydrolysis. However, it was necessary in this case to add 100 ml. of 10% hydrochloric acid to completely hydrolyze the complex.

The ether layer was separated, washed with sodium bicarbonate solution and water, dried over sodium sulfate, and then evaporated in vacuo. The concentrated ether solution was poured into petroleum ether, whereupon an oil separated. The oil soon solidified to yield 32.0 grams of crude product. Recrystallizing this product from benzene yielded a material melting at 82-83° and a second crystallization from carbon tetrachloride gave crystals that melted at 83.5-84.5°. The melting point of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol reported by Roberti, et al. (17) was 84-85°. An attempt to purify the crude product by distillation caused dehydration and the formation of isoeugenol.

SYNTHESIS OF 1-(4-BENZOXY-3-METHOXYPHENYL)-1-PROPANOL (II)



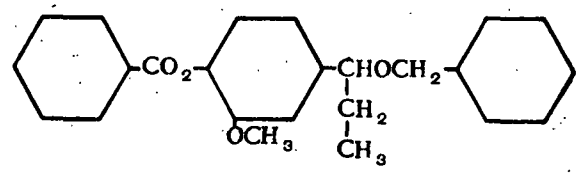
(II)

The benzoate (II) was prepared according to the well-known general method of esterification given by Schotten and Bauman.

1-(4-hydroxy-3-methoxyphenyl)-1-propanol (5 grams) was dissolved in 100 ml. of 5% sodium hydroxide solution. Benzoyl chloride was added at intervals and the mixture was shaken vigorously. The solid ester separated and was filtered. After repeated crystallization of the product from dilute ethanol, 5.5 grams of the pure benzoate were obtained; the melting point was 126-128°.

Analysis: Calculated for 1-(4-benzoxy-3-methoxyphenyl)-1-propanol, $C_{17}H_{18}O_4$: MeO, 10.9%. Found: MeO, 11.1%.

REACTION OF 1-(4-BENZOXY-3-METHOXYPHENYL)-1-PROPANOL WITH BENZYL CHLORIDE

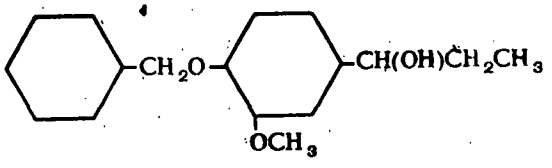


(III)

In an attempt to prepare 1-benzyloxy-1-(4-benzoxy-3-methoxyphenyl)-propane (III), benzyl chloride was reacted with 1-(4-benzoxy-3-methoxyphenyl)-1-propanol (II) in the presence of anhydrous potassium carbonate. The reaction conditions were chosen as a result of recent benzylating experiments reported in the literature. In one experiment Weygand and Trauth (18) formed a tribenzylglucose derivative by heating a benzyl chloride solution of monoacetoneglucose in the presence of pulverized potassium hydroxide. Freudenberg and Bittner (19) obtained a benzyl ether by refluxing a phenol in anhydrous methyl alcohol with benzyl chloride and potassium carbonate.

Although the procedure of Weygand and Trauth (18) yielded a benzyl ether of an aliphatic alcohol, it seemed certain that the strong conditions--i.e., heating in the presence of potassium hydroxide--would saponify a benzoyl ester. The conditions employed by Freudenberg and Bittner (19), although not shown to form a benzyl ether of an aliphatic alcohol, appeared less apt to saponify a benzoate.

Equimolar amounts of 1-(4-benzoxy-3-methoxyphenyl)-1-propanol (10 grams) and benzyl chloride (4.4 grams) were refluxed in 100 ml. of anhydrous methyl alcohol with 10 grams of potassium carbonate for 24 hours. The mixture was poured into ice water and the product was extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and evaporated in vacuo. The resulting oil could not be crystallized. This material was boiled in alcoholic potassium hydroxide for one hour, poured into water, and extracted with ether. The ether extract was washed with water, dried over sodium sulfate, and evaporated in vacuo to yield an oil which crystallized on standing. Approximately six grams of crude product were obtained. The product was recrystallized from a benzene-petroleum ether solution to yield needles melting at 61-65°. A second crystallization gave needles melting at 63-65°. Analysis indicated that this compound was 1-(4-benzyloxy-3-methoxyphenyl)-1-propanol (IV).



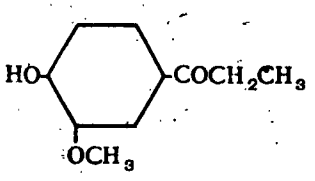
(IV)

Analysis: Calculated for 1-(4-benzyloxy-3-methoxyphenyl)-1-propanol (IV), $C_{17}H_{20}O_3$: MeO, 11.4%. Found: MeO 11.5%.

The benzyl ether (IV) was also prepared in a conventional manner. Benzyl chloride (2.09 grams) was refluxed with 3.0 grams of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol and 0.93 gram of potassium hydroxide in 40 ml. of absolute ethanol. After refluxing 30 minutes, potassium chloride ceased to

precipitate. The mixture was poured into ice water and an oil separated. The oil solidified almost immediately when a few crystals of the above benzyl ether were added. The white solid product was filtered, washed with water, with 2% sodium hydroxide solution and, finally, with water. Three grams of white material were obtained that melted at 63-65°. Recrystallization from a benzene-petroleum ether solution yielded needles that melted at 63-65° and gave no depression in a mixed melting point with the benzyl ether described above.

SYNTHESIS OF PROPIOVANILLINE (V)



(V)

Two procedures were available for the preparation of propiovanillone. Johnson and Hodge (20) employed the Friedel-Crafts reaction with veratrole and propionyl chloride. Coulthard, Marshall, and Pyman (21) obtained propiovanillone from a Fries rearrangement of 2-methoxyphenyl propionate. The method of Coulthard, et al. was selected because a higher yield was expected.

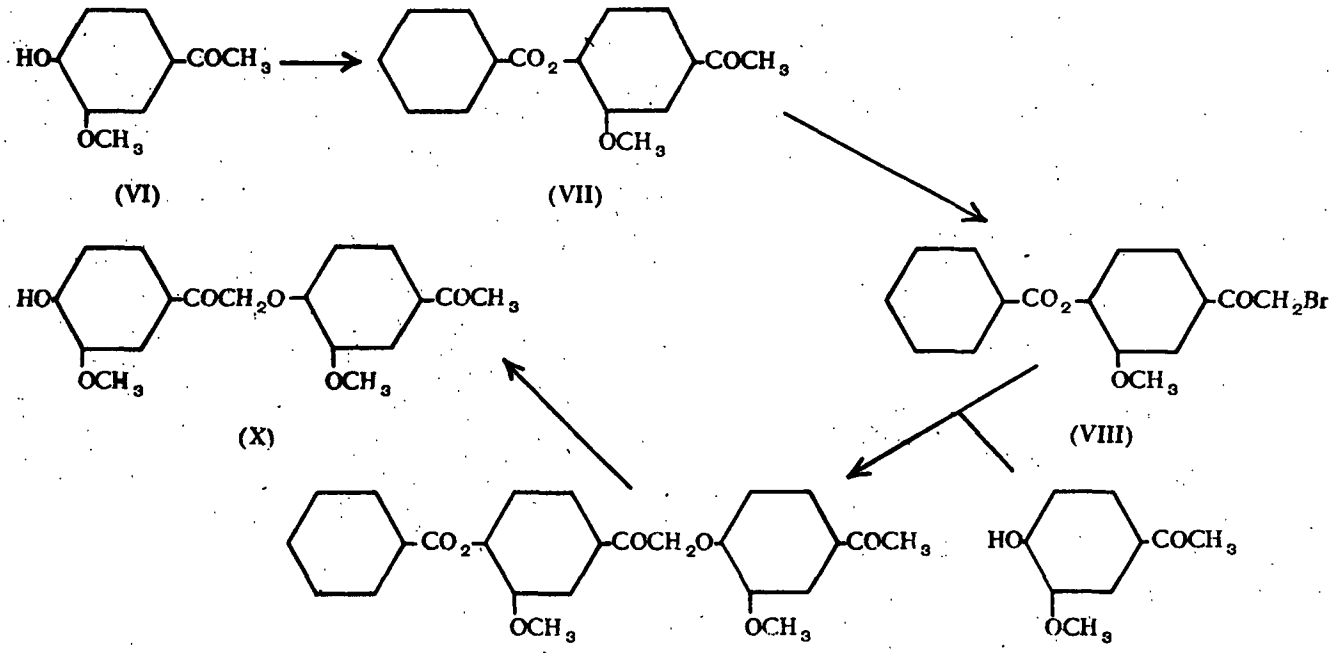
Guaiacol (124 grams) and 92.3 grams of propionyl chloride were heatedon a steam bath for one hour. After hydrogen chloride evolution was complete, the liquid was distilled under vacuum. A 152-gram fraction was obtained that distilled between 120-126° at 10 mm. pressure.

The ester was added rapidly to a cold solution (10°) containing 510 ml. of nitrobenzene and 224 grams of anhydrous aluminum chloride. The mixture was swirled until it became viscous. It was then heated for 1.5 hours in an

oil bath at 80° and allowed to stand overnight. The red-brown solid complex that separated was filtered and washed successively with benzene, benzene-petroleum ether, and low boiling petroleum ether. The light brown solid was dried in a desiccator and then hydrolyzed with dilute hydrochloric acid. The oil which separated crystallized to yield 70 grams of crude product. The solid was recrystallized from benzene-petroleum ether. A second crystallization from benzene yielded crystals melting at 60.5-61°. Coulthard, et al. (21) reported the melting point of propiovanillone to be 61-62°.

ω-(4-ACETYL-2-METHOXYPHENOXY)ACETOVANILLONE (X)

The method of Erdtman and Leopold (22) was used for all reactions leading to the preparation of ω-(4-acetyl-2-methoxyphenoxy)acetovanillone (X).



Synthesis of Acetovanillone Benzoate

Fifty grams of acetovanillone (VI) and benzoyl chloride (42.1 grams) were refluxed in 100 ml. of pyridine for 30 minutes and poured into ice water

The solid product was filtered and washed with sodium carbonate solution and hot water to yield 80 grams of material. Recrystallization from benzene-petroleum ether gave needles melting at 107.5-108°. Erdtman and Leopold (22) reported the melting point of acetovanillone benzoate to be 108-109°.

Synthesis of ω-Bromoacetovanillone Benzoate (VIII)

Acetovanillone benzoate (70 grams) was dissolved in 300 ml. of chloroform and brominated with 42.5 grams of bromine in 200 ml. of chloroform. The bromine solution was added in small portions, allowing the red color to disappear after each addition. The chloroform solution was poured into ice water and the chloroform layer was washed twice with sodium bicarbonate solution and once with water. Evaporation of the chloroform yielded a solid product. Recrystallization from 95% ethanol gave 64 grams of crystals melting at 101-102°. The material gave a positive Beilstein test for halogens. Erdtman and Leopold (22) reported the melting point of ω-bromoacetovanillone benzoate to be 105-106°.

Synthesis of ω-(4-Acetyl-2-methoxyphenoxy)acetovanillone Benzoate (IX)

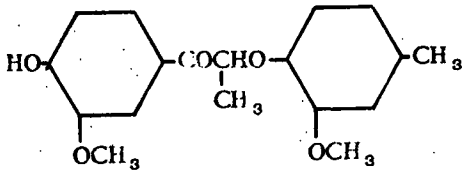
Acetovanillone (9.5 grams) and ω-bromoacetovanillone benzoate (20 grams) were refluxed in 200 ml. of methyl ethyl ketone with 30 grams of anhydrous potassium carbonate for 30 minutes. (Very little potassium bromide was precipitated after 20 minutes of refluxing.) The mixture was poured into ice water and acidified with dilute sulfuric acid. The oil that separated was removed and the water layer was extracted with ether. The oil and ether extract were combined, dried over sodium sulfate, and evaporated in vacuo to yield an oily product. The product crystallized when triturated with a small amount of methyl alcohol. Approximately 20 grams of crude material were obtained. After three crystallizations from methyl alcohol a product was obtained that

melted at 137.5-138°. Erdtman and Leopold (22) reported the melting point of ω-(4-acetyl-2-methoxyphenoxy)acetovanillone benzoate to be 138-139°.

Synthesis of ω-(4-Acetyl-2-methoxyphenoxy)acetovanillone (X)

An absolute ethanol solution (100 ml.) containing 9.6 grams of the benzoate (IX) and 4.0 grams of piperidine was refluxed for 30 minutes and poured into water. The mixture was acidified and extracted with chloroform. The chloroform solution was dried over sodium sulfate, filtered through a column containing aluminum oxide, and evaporated to yield an oily solid. The solid product (5.4 grams) that remained after washing with ether melted at 130-134°. Recrystallization from methyl alcohol yielded crystals melting at 139-142°. The final product (4.6 grams) was soluble in alkali and gave a phenolic test with ferric chloride solution. The melting point reported by Erdtman and Leopold (22) for ω-(4-acetyl-2-methoxyphenoxy)acetovanillone was 140-142°.

ATTEMPTED SYNTHESIS OF α-(2-METHOXY-4-METHYLPHENOXY)PROPIOVANILLONE (XV)

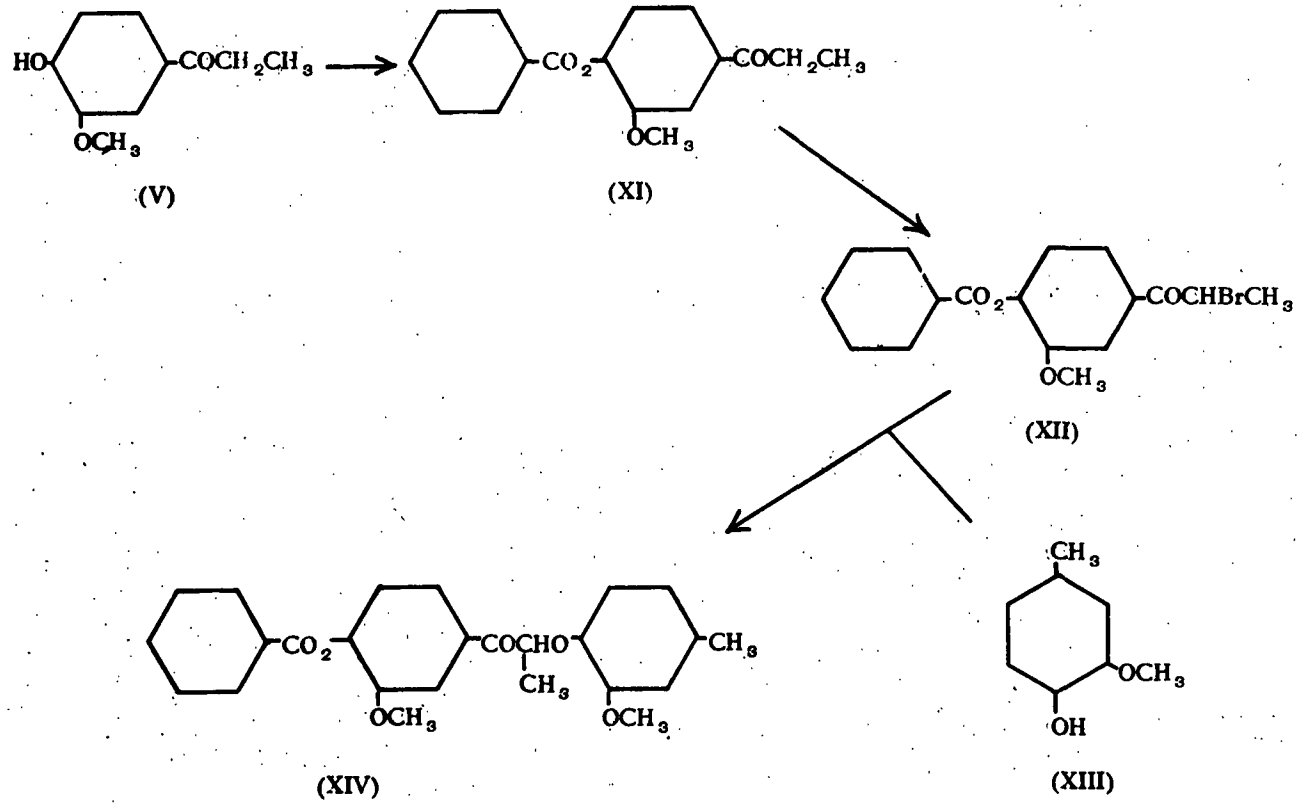


(XV)

In an attempt to prepare α-(2-methoxy-4-methylphenoxy)propiovanillone (XV), α-bromopropiovanillone benzoate (XII) was treated with creosol (XIII), using the same conditions that were employed in the preparation of ω-(4-acetyl-2-methoxyphenoxy)acetovanillone benzoate (IX). The reaction failed to proceed in the desired manner because creosol benzoate was obtained as a

product instead of α-(2-methoxy-4-methylphenoxy)propiovanillone benzoate (XIV). The reaction was repeated using acetovanillone in place of creosol. Trans-esterification evidently occurred again, because acetovanillone benzoate was isolated as the main product.

Acetovanillone was substituted for creosol in the above reaction, because its reactivity was shown to be different from that of creosol in the ether synthesis. This was shown by comparing the reactions of creosol and aceto-vanillone with ω-bromoacetovanillone benzoate. In the case of acetovanillone, the reaction went to completion within 20 minutes, whereas the reaction of creosol was only slight after 12 hours. The rate of reaction was judged by the amount of potassium bromide precipitated. 4-Ethylguaiacol was similar to creosol in that it reacted very slowly with ω-bromoacetovanillone benzoate.



Synthesis of Propiovanillone Benzoate (XI)

A 20% sodium hydroxide solution (500 ml.) containing 17.2 grams of propiovanillone (V) was shaken vigorously with 80 grams of benzoyl chloride. The solid ester that separated was filtered, dried, and crystallized from absolute ethanol to yield crystals melting at 106-107°. A second crystallization from benzene-petroleum ether gave a product melting at 107.5-108°. Coulthard, et al. (21) reported the melting point of propiovanillone benzoate to be 108-110°.

Synthesis of α-Bromopropiovanillone Benzoate (XII)

Propiovanillone benzoate (20.4 grams) was dissolved in 200 ml. of chloroform and was brominated with 11.6 grams of bromine dissolved in 50 ml. of chloroform. The procedure employed was the same as that used in preparing ω-bromoacetovanillone benzoate. Recrystallization of the crude product from absolute ethanol yielded 22.7 grams of material melting at 131-132°. A second crystallization gave white granular crystals melting at 135-136°. The product gave a positive Beilstein test for halogens.

Analysis: Calculated for α-bromopropiovanillone benzoate, $C_{17}H_{15}O_4Br$: MeO, 8.54%. Found: MeO, 8.7%.

Reaction of α-Bromopropiovanillone Benzoate with Creosol

Creosol (XIII)(7.6 grams) and 20 grams of α-bromopropiovanillone benzoate (XII) were refluxed with 30 grams of potassium carbonate in 250 ml. of methyl ethyl ketone for 30 minutes. The mixture was poured into ice water, acidified, and extracted with ether. The ether extract was dried over sodium sulfate and evaporated to yield an oily solid. A small amount of the product was recrystallized twice from absolute methanol to yield crystals melting at 133-135°. The crystals gave no depression in a mixed melting point with α-bromopropiovanillone benzoate.

The oily solid was combined with 10 ml. of creosol and refluxed with 30 grams of potassium carbonate in 200 ml. of methyl ethyl ketone for six hours. (The solution darkened considerably during the latter two hours.) The mixture was poured into ice water, acidified with dilute sulfuric acid, and extracted with ether. The ether extract was washed with sodium bicarbonate solution and water, dried over sodium sulfate, and evaporated to yield a solid. The solid was recrystallized twice from dilute methanol to yield 7.0 grams of crystals melting at 71-72.5°. The product gave no depression in a mixed melting point with creosol benzoate.

Analysis: Calculated for creosol benzoate, $C_{15}H_{14}O_3$: MeO, 12.8%. Found: MeO, 12.8%.

Synthesis of Creosol Benzoate

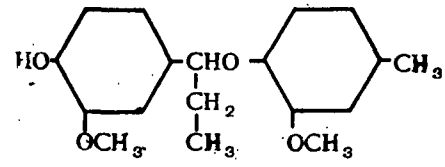
Creosol (5.0 grams) and 5.1 grams of benzoyl chloride were refluxed in 40 ml. of pyridine for 15 minutes. The solution was poured into ice water, upon which a white product separated. The mixture was filtered to yield 7.4 grams of product melting at 64-68°. Recrystallization from dilute methanol gave crystals melting at 71-72.5°. The melting point of creosol benzoate has been reported to be 75° (22a).

Reaction of α-Bromopropiovanillone Benzoate with Acetovanillone

Acetovanillone (18.3 grams) and 20 grams of α-bromopropiovanillone benzoate were refluxed with 30 grams of potassium carbonate in 200 ml. of methyl ethyl ketone for 45 minutes. The mixture was poured into ice water and extracted with ether. The ether extract was washed successively with 2% sodium hydroxide solution and water, dried over sodium sulfate, and evaporated to yield approximately 18 grams of sticky solid. The solid product was recrystallized from butyl alcohol to yield crystals melting at

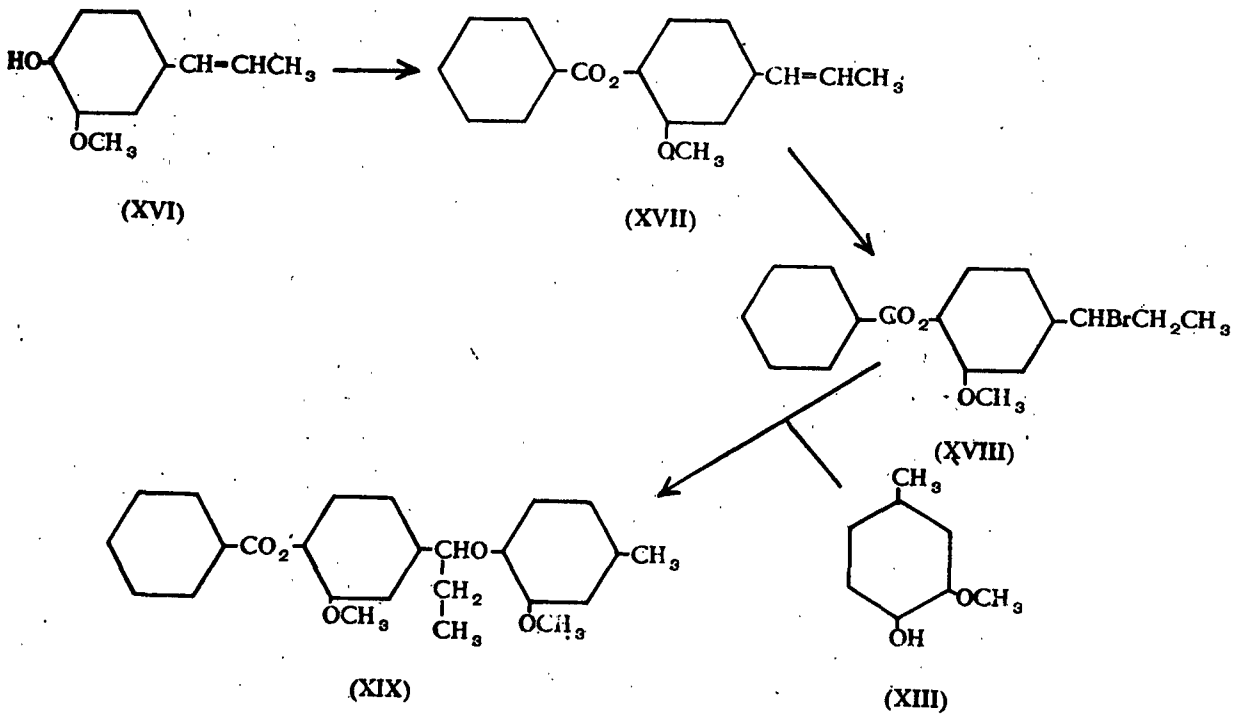
103.5-105°. A second crystallization from benzene-petroleum ether gave a product melting at 106-107.5°. A mixed melting point with acetovanillone benzoate (m.p. 107.5-108°) gave no depression.

ATTEMPTED SYNTHESIS OF 4-[1-(2-METHOXY-4-METHYLPHENOXY)PROPYL]GUAIACOL (XX)



(XX)

In an attempt to prepare the ether (XX), creosol (XIII) was reacted with 1-(4-benzoxy-3-methoxyphenyl)-1-bromopropane (XVIII). Although various conditions were used, the desired product was not isolated. In reactions where the starting materials were not recovered, saponification of the benzoyl group was indicated because very little alkali-insoluble material was obtained:



(XVI) (XVII) (XVIII) (XIX) (XIII)

Isoeugenol (XVI) (51.5 grams) and 45 grams of benzoyl chloride were refluxed in 100 ml. of pyridine for one hour and poured into a cold 5% sulfuric acid solution. The oil that separated was stirred until it solidified. The solid product was filtered to yield 55.8 grams of material melting at 96-101°. Repeated crystallization from 95% ethanol gave a product melting at 102-103°. Tiemann (23) reported the melting point of isoeugenol benzoate to be 103-104°.

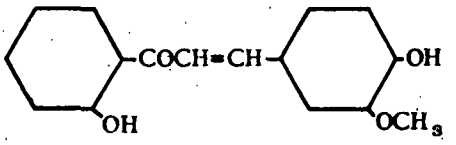
Synthesis of 1-(4-Benzoxy-3-methoxyphenyl)-1-bromopropane (XVI)

Isoeugenol benzoate (40 grams) was dissolved in 180 ml. of chloroform and cooled in an ice bath. A 30% hydrobromic acid solution in acetic acid (250 grams) was added rapidly, and the solution was allowed to react at room temperature for two days. The dark violet solution was poured into ice water and the chloroform layer was separated. After the chloroform solution was washed twice with sodium bicarbonate solution and once with water, it was dried over sodium sulfate and evaporated in vacuo. The resulting solid was crystallized from absolute ethanol to yield 30 grams of product melting at 107-108.5°. The crystals obtained after a second crystallization from ethanol melted at 109-109.5°. When the ethanol solution was heated to dissolve the compound, considerable darkening occurred. Prolonged heating caused a dark oil to separate with the crystals on cooling. The material was again recrystallized from 1:5 chloroform-petroleum ether. No darkening occurred and white crystalline leaflets melting at 109.5-111° were obtained. The material gave a positive Beilstein test for halogens. Analysis of the compound indicated a monobromo derivative of isoeugenol benzoate. The melting point of the isomeric 1-(4-benzoxy-3-methoxyphenyl)-2-bromopropane has been reported to be 80° (24). The compound was also converted to 1-(4-benzoxy-

3-methoxyphenyl)-1-propanol by refluxing with an alcoholic solution of sodium thiosulfate. Therefore, the compound must be 1-(4-benzoxy-3-methoxyphenyl)-1-bromopropane.

Analysis: Calculated for 1-(4-benzoxy-3-methoxyphenyl)-1-bromopropane, $C_{17}H_{17}O_3Br$: C, 58.40%; H, 4.87%; MeO, 8.9%. Found: C, 58.35%; H, 4.89%; MeO, 8.9%.

SYNTHESIS OF 2',4-DIHYDROXY-3-METHOXYCHALCONE (XXI)



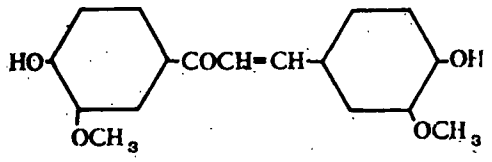
(XXI)

Russell and Todd (25) prepared 2',4-dihydroxy-3-methoxychalcone by passing dry hydrogen chloride through an ethyl acetate solution containing vanillin and o-hydroxyacetophenone. Sen (14) repeated the preparation, using the method of Russell and Todd, but obtained only a low yield of the chalcone. By reacting an alcoholic solution of vanillin and o-hydroxyacetophenone with alkali, Sen was able to obtain a much higher yield. Sen's method was chosen for this synthesis.

Vanillin (60.8 grams) and o-hydroxyacetophenone (54.4 grams) were dissolved in 200 ml. of absolute ethanol and cooled to 0°. A 300 ml. solution of 60% potassium hydroxide, cooled to 0°, was added to the above solution with stirring. The flask was stoppered and allowed to stand for three weeks with occasional shaking. The resulting semisolid oil was poured into ice water and acidified with 6 N hydrochloric acid. It was then extracted with ether, washed with sodium bisulfite solution, and subjected to steam

distillation to remove excess o-hydroxyacetophenone. The resulting solid was crystallized from dilute ethanol to yield 37.0 grams of yellow needles melting at 126-128°. Russell and Todd (25) and Sen (14) reported the melting point of 2',4-dihydroxy-3-methoxychalcone to be 129°.

SYNTHESIS OF 4,4'-DIHYDROXY-3,3'-DIMETHOXYCHALCONE (XXII)

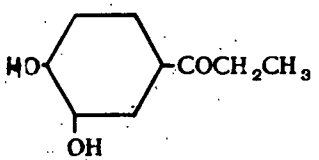


(XXII)

The preparation of 4,4'-dihydroxy-3,3'-dimethoxychalcone was carried out according to the method of Pearl and Dickey (26).

Acetovanillone (49.8 grams) and vanillin (45.6 grams) were dissolved in 900 ml. of absolute ethanol and cooled in an ice-salt bath. Anhydrous hydrogen chloride gas was passed through the solution for one hour. The purple precipitate that formed was filtered and, when stirred into water, the material turned yellow. The yellow product was recrystallized from dilute ethanol to yield 76 grams melting at 116-118°. A second crystallization gave a yellow product melting at 118-120°. Pearl and Dickey (26) reported the melting point of 4,4'-dihydroxy-3,3'-dimethoxychalcone to be 118-120°.

SYNTHESIS OF 4-PROPIONYLPYROCATECHOL (XXIII)



(XXIII)

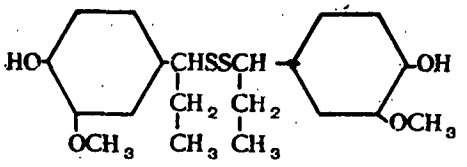
4-Propionylpyrocatechol was prepared according to the procedure given by Rosenmund and Lohfert (27).

Catechol (13.0 grams) and propionyl chloride (20 grams) were heated on a steam bath for one hour. The resulting solution was dissolved in ether, washed with 2% sodium hydroxide solution, and dried over sodium sulfate. After the ether was removed by evaporation, the resulting oil was distilled in vacuo. Catechol dipropionate (16.0 grams) was collected from 164-166° at 16 mm.

The ester (15.0 grams) was added to a cooled solution of 36.0 grams of aluminum chloride in 60 ml. of nitrobenzene. (A 4:1 mole ratio of aluminum chloride to the ester was used.) After standing for 45 hours, the mixture was heated on a steam bath for one hour. The nitrobenzene was then removed by steam distillation. The nonvolative residue consisted of an aqueous layer and a dark oil. On cooling, white crystals formed in the aqueous layer and the dark oil solidified. Approximately 4.5 grams of white crystals, melting at 141-145°, were obtained. The dark material (11.0 grams) was boiled in water, and the water was decanted to avoid the dark insoluble residue. Approximately two grams of light colored crystals separated on cooling the aqueous solution.

The crystalline material was combined, dissolved in hot water, and boiled with decolorizing carbon. On cooling the filtered aqueous solution, two batches of light colored crystals were obtained; the first batch (2.5 grams) melted at 144.5-146°, and the second batch (2.3 grams) melted at 142-145°. Rosenmund and Lohfert (27) reported the melting point of 4-propionylpyrocatechol to be 146°.

SYNTHESIS OF BIS[1-(4-HYDROXY-3-METHOXYPHENYL)-1-PROPYL] DISULFIDE (XXIV)



(XXIV)

A solution of 25 ml. of absolute ethanol containing 0.5 gram of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol was maintained saturated with hydrogen sulfide while 20 grams of a 50% potassium hydroxide solution were added dropwise. The solution was diluted with 50 ml. of water and again saturated with hydrogen sulfide. The solution was allowed to stand overnight and then filtered to remove a slight amount of turbidity. Needles formed during a period of a week and were filtered to yield 0.1 gram of crystals. The mother liquor was saturated with hydrogen sulfide and an additional 0.05 gram of crystals formed during the following week. After the solution was filtered for the second time and stored in a stoppered bottle, relatively few crystals formed during a period of two weeks. The stopper was removed and air was bubbled through the solution for a few minutes. Within 24 hours, an additional 0.25 gram of white needles formed.

The crystalline material melted at 113-115°. Repeated crystallization from dilute ethanol yielded crystals that melted at 115-117° and gave no depression in a mixed melting point with bis[1-(4-hydroxy-3-methoxyphenyl)-1-propyl] disulfide as obtained in the cooking experiments.

REACTION OF ISOLATED NATIVE LIGNIN WITH POTASSIUM HYDROSULFIDE

A solution of 50 ml. of 95% ethanol containing one gram of spruce isolated native lignin [prepared by F. E. Brauns (1)] (MeO, 14.8%) was maintained saturated with hydrogen sulfide while 20 grams of a 50% potassium hydroxide solution were added dropwise. A precipitate formed when the first few drops of potassium hydroxide solution were added but it redissolved as the addition of alkali was continued. A clear red solution was obtained when all the potassium hydroxide had been added and the solution was saturated with hydrogen sulfide. The solution was stored in a stoppered flask for three weeks.

A clear solution resulted when the alcoholic solution was diluted with twice its volume of water. A precipitate formed when the alcohol was evaporated in vacuo. A stream of hydrogen sulfide was introduced during the evaporation. The precipitate was filtered to yield 0.20 gram of light colored product. A stream of carbon dioxide was bubbled through the orange colored filtrate for 12 hours. At the end of that time, considerable precipitate had formed; the yield was 0.55 gram of material. The yellow colored filtrate was acidified with dilute sulfuric acid and the precipitate that formed was filtered (0.3 gram).

Each of the above fractions was dried in a desiccator and then dissolved in dioxane. Considerable free sulfur was present in the second fraction; the third fraction was almost pure sulfur. The dioxane solutions were filtered and then treated twice with mercury to remove any free sulfur. In order to insure enough material for analysis, the dioxane

solutions were filtered and then treated twice with mercury to remove any free sulfur. In order to insure enough material for analysis, the dioxane solutions of fraction one and two were combined and concentrated by evaporating in vacuo. The concentrated solution was poured into ether, whereupon a light colored material precipitated. The mixture was centrifuged and the clear solution was decanted. The precipitate was stirred in petroleum ether (30-60°) and the mixture was again centrifuged. The petroleum ether was decanted and the precipitate dried to a light colored powder. A qualitative test indicated the presence of sulfur.

Analysis: MeO, 13.8%; S, 3.4%.

SODIUM HYDROSULFIDE COOKS

COOKING LIQUOR

The primary purpose of this investigation was to gain an insight into the formation of thiolignin. Accordingly, it seemed advantageous to accentuate as far as possible the role of the sulfide ion in the cooking liquor. The use of a regular kraft cooking liquor was not suitable because the action of the alkali in great excess would overshadow the action of the sulfide ion. On the other hand hydrogen sulfide was not desirable because of the vast differences between acid and alkaline cooking liquors. A sodium hydrosulfide solution appeared to serve most satisfactorily as a cooking liquor. However, the neutral or near neutral sodium hydrosulfide solutions (pH 7.0 or 8.1) used by Enkvist (16) were not considered sufficiently alkaline to represent the actions of the reagent in the kraft cook.

Two cooking liquors were prepared for the experimental cooks. Liquor A contained 1.66 moles of sulfur per liter (as sulfide and hydrosulfide, determined by titration with standard iodine solution) and 1.76 moles of sodium per liter (determined by titration with standard hydrochloric acid to a methyl orange end point); the pH was 12.3 at 22°. Liquor B contained 1.30 moles of sulfur per liter and 1.75 moles of sodium per liter; the pH was 12.9 at 22°.

During the initial experimental cooks it was found that sodium hydrosulfide solution A would not always completely dissolve the model compounds. When the cook was carried out with part of the compound undissolved, a residue formed that was very resinous and could not be characterized. On the other hand, no insoluble residues formed when the more alkaline liquor B was used.

In order to compare the effects of using either liquor A or B, the cooks with 2',4-dihydroxy-3-methoxychalcone can serve as an example. Approximately 150 ml. of liquor A were required to dissolve 2.0 grams of the chalcone, whereas 4.0 grams of the compound were easily dissolved in 80 ml. of cooking liquor B. A residue did not form in either cook and the yields of vanillin were approximately the same. When 8.0 grams of the chalcone were cooked with 240 ml. of cooking liquor A, it was only partially dissolved and a gummy residue formed.

Because of the ease of polymerizing phenolic materials, especially when heated in a solid state, it was decided that the more alkaline liquor B, which kept the phenolic compounds in solution, was preferred. Therefore,

instead of using a sodium hydrosulfide liquor (solution A), a liquor was chosen that contained one mole of sodium sulfide and two moles of sodium hydrosulfide (solution B).

GENERAL PROCEDURES

The Cooking Procedure

A 300-ml. stainless steel autoclave was used for all cooks. It was equipped with a pressure gage, a thermometer well, and a valve for relieving gases. The autoclave fitted snuggly into a Glas-col heating mantle (600-ml. beaker size). The entire unit was mounted on a shaker to insure continuous mixing.

The model compounds were cooked four to five hours at 160°. Approximately two hours were required to reach maximum temperature and the autoclave was allowed to cool overnight after the cooking period. Gases were relieved from the autoclave at 105°.

The Isolation of Reaction Products

The contents of the autoclave were transferred to a separatory funnel and saturated with sodium chloride and hydrogen sulfide. The neutral solution was then extracted with ether three times. The ether extract was washed with water, dried over sodium sulfate, and evaporated *in vacuo*. In some cases, a stream of carbon dioxide or nitrogen was passed through the solution during evaporation.

The reaction products obtained by using the above procedure were not contaminated with free sulfur. When hydrochloric acid or carbon dioxide

was used to neutralize the alkaline liquor, considerable free sulfur was present with the isolated products. Evidently sulfur was soluble in the solution neutralized with hydrogen sulfide and was not extracted in appreciable quantities by the ether.

Chromatographic Separations of the Reaction Products

In several cases, the isolated reaction products were separated by using chromatographic techniques. The procedure involved chromatographing a benzene solution of the product mixture on an acid-washed Magnesol column (28). A benzene-absolute ethanol solution was used as a developer. After extrusion, the column was streaked with the following streak reagents (28): ferric chloride, 2,4-dinitrophenylhydrazine, and alkaline potassium permanganate. The different zones indicated by the streaking reagents were separated and eluted with acetone.

Prior to carrying out a full-scale chromatographic separation of the entire mixture, it was necessary to run several preliminary chromatograms in order to establish developing conditions. The preliminary chromatograms were run on a No. 1 column, using 10-20 mg. of the product mixture and one column length of 100°:1 benzene-absolute ethanol as a developer. (The amount of developer necessary to completely wet the packed column was considered one column length of developer.) Depending upon the type of separations obtained on a No. 1 column, the developing conditions were modified by changing the ratio of benzene to absolute ethanol and/or by varying the amount of developer used. Column sizes are listed in Table I.

TABLE I

CHROMATOGRAPHIC COLUMN SIZES

Column Size	Diameter, mm.	Length of Magnesol Column, cm.	Volume of Developer Equivalent to One Column Length, ml.
1	11	11	8
2	19	17	30
3	38	19	120
4	48	23	210

PROPIOVANILLONE

Propiovanillone was cooked by the regular procedure described above. It was also cooked over an extended time to determine the effects of prolonged cooking.

Regular Cook

Propiovanillone (2.0 grams) was cooked in 60 ml. of cooking liquor A* for five hours at 160°. The reaction product (1.7 grams) was isolated by the general techniques described above. The product was an oil that crystallized on standing. The crude material melted at 48-55°. Although the product had a slight garlic or kraft odor, a microqualitative sulfur test did not indicate the presence of sulfur.

A benzene solution containing 1.6 grams of the crude product was chromatographed on a No. 3 column, using two column lengths of 100:1 benzene-

*Liquor B was not adopted as the regular cooking liquor until after this cook.

absolute ethanol as a developer. After extrusion, the column was streaked and two zones were indicated. The results of the chromatographic separation are given below.

Zone	Streaking Results	Recovered Material g.	Recovered Material %
A	Green ferric chloride Reduced permanganate	0.15	9.4
B	Reduced permanganate	1.40	87.5
		1.55	96.9

Zone A yielded 0.15 gram of a dark oil that partially crystallized. The crystals melted at 112-116° (Fischer-Johns melting point apparatus). The crystals were very soluble in 95% ethanol, difficultly soluble in benzene, and soluble in hot water. They were washed free of the dark oil with benzene and recrystallized from water. The light colored product softened at 130° (capillary) but main melting occurred at 142-144°. Insufficient material was available to accomplish a second crystallization. A mixed melting point with an authentic sample of 4-propionylpyrocatechol (m.p. 144.5-146°) gave inconclusive results because softening occurred at 130° and the mixture melted at 142-145°. Coulthard, et al. (21) described 4-propionylpyrocatechol as being soluble in hot water and difficultly soluble in benzene. On the basis of the green ferric chloride test and other physical properties of the product, it was evidently 4-propionylpyrocatechol.

Zone B yielded a colorless oil that completely solidified when rubbed with a stirring rod. The white powder obtained melted at 58-60°.

After recrystallizing from benzene-petroleum ether, long needles were obtained which melted at 58.5-60.5° and gave no depression in a mixed melting point with propiovanillone.

Extended Cook

Propiovanillone (3.0 grams) was cooked in 60 ml. of cooking liquor B for 30 hours at 160°. Isolation of the product by the general procedure yielded 2.8 grams of crystalline material. The crystals were washed with a small amount of benzene; 0.3 gram of the crystals remaining was filtered and melted at 128-142°. Recrystallization from water yielded 0.2 gram of light colored material melting at 144-146°. A mixed melting point with 4-propionylpyrocatechol gave no depression.

The benzene solution was chromatographed, using a 200:1 benzene-absolute ethanol solution as a developer. A chromatogram was obtained that was similar to the one described above. In this case, the lower zone yielded 2.1 grams of propiovanillone, which melted at 58-60°. The other fraction, a partially crystallized oil, was washed with benzene to yield 0.2 gram of material melting at 132-141°. Recrystallization from water gave 0.15 gram of yellow crystals melting at 143.5-145°. A mixed melting point with 4-propionylpyrocatechol gave no depression.

Analysis of the yellow crystals: Calculated for 4-propionylpyrocatechol, $C_9H_{10}O_3$: C, 65.04%; H, 6.07%. Found: C, 65.08%; H, 6.11%.

2',4-DIHYDROXY-3-METHOXYCHALCONE

2',4-Dihydroxy-3-methoxychalcone (4.0 grams) was cooked in 80 ml. of cooking liquor B for 4.5 hours at 160°. By using the general procedure,

approximately 4.0 grams of partially crystallized oil were obtained as a product. The product did not have a typical kraft odor.

A benzene solution of the product was chromatographed on a No. 4 column, using one and one-half column lengths of 200:1 benzene-absolute ethanol as a developer. After extruding the column and streaking, the zones listed below were obtained.

Zone	Streaking Results	Recovered Material g.	%
A	Dark colored	nil	- -
B	Green ferric chloride Brown 2,4-D.P.H.*	0.20	5.0
C	Yellow colored	0.20	5.0
D	Orange 2,4-D.P.H.*	1.60	40.0
E	Yellow colored	0.40	10.0
F	Violet ferric chloride	1.40	35.0
		3.80	95.0

*2,4-dinitrophenylhydrazine

The material from zone B was a dark, partially crystallized oil. The crystals melted at 139-149° (Fischer-Johns melting point apparatus). The material after recrystallizing from xylene melted at 145-150°. A second crystallization from water gave a light colored product melting at 148-153°. This crystalline material was then boiled in ethanol with decolorizing carbon and, after filtering, the alcohol was evaporated to yield a white product melting at 147-151°. Recrystallizing this product from benzene produced crystals that melted at 151-153° and gave no depression in

a mixed melting point with an authentic sample of protocatechualdehyde (m.p. 151-153°). The product also gave a strong green color with ferric chloride.

Zone D yielded a light yellow crystalline material melting at 71-77°. The material was recrystallized from petroleum ether (60-110°) to yield 1.2 grams of fluffy needles melting at 78-80°. A mixed melting point with vanillin gave no depression. A small amount of yellow oil, insoluble in the boiling petroleum ether, was combined with the material from zone E. An ether solution of the combined material was extracted with 21% sodium bisulfite solution and then evaporated. The resulting yellow crystalline material (0.3 gram) melted at 110-124°. Recrystallizing from dilute ethanol yielded yellow needles that melted at 125-127° and gave no depression in a mixed melting point with 2',4-dihydroxy-3-methoxychalcone.

A paper chromatogram, using butanol saturated with 2% aqueous ammonia as a developer, indicated that the material in zone C was mainly vanillin with a small amount of the unreacted chalcone.

The oil obtained from zone F had the odor of o-hydroxyacetophenone. The acetate was prepared by dissolving the oil in pyridine, adding an excess of acetic anhydride, and allowing the solution to react overnight. A solid product was obtained when the solution was poured into ice water. The crude acetate (1.1 grams) melted at 80-86°. Recrystallizing from dilute ethanol yielded crystals melting at 87-88.5°. A mixed melting point with an authentic sample of o-acetoxyacetophenone gave no depression.

4,4'-DIHYDROXY-3,3'-DIMETHOXYCHALCONE

4,4'-Dihydroxy-3,3'-dimethoxychalcone (5.0 grams) was cooked in 100 ml. of liquor B for 4.5 hours at 160°. The product was isolated in the regular manner; the yield was 5.05 grams of crystalline material.

A benzene solution of the products (5.0 grams) was chromatographed on a No. 4 column, using four column lengths of 250:1 benzene-ethanol solution as a developer. The results of the chromatographic separation are listed below.

Zone	Streaking Results	Recovered Material g.	%
A	Green ferric chloride Brown 2,4-D.P.H.	0.30	6.0
B	Yellow colored band	0.20	4.0
C	Orange 2,4-D.P.H.	3.90	78.0
D	Thin dark colored band	0.10	2.0
		4.50	90.0

Zone A yielded a partially crystallized oil. The location of the zone and the green ferric chloride color test indicated the presence of demethylated products. (A chromatogram of the product from cooking 2',4-dihydroxy-3-methoxychalcone yielded protocatechualdehyde from a zone similar to zone A.) In this cook the demethylated products could be derivatives of both vanillin and acetovanillone. Because no suitable technique was available for separating 4-acetopyrocatechol and protocatechualdehyde, the relatively small amount of product was not characterized.

The yellow oil from zone B was dissolved in hot ethanol and diluted with water. On cooling yellow crystals formed that melted at 112-116°. Recrystallization from dilute ethanol yielded a yellow material melting at 116-119° that gave no depression in a mixed melting point with 4,4'-dihydroxy-3,3'-dimethoxychalcone.

The crystalline material from zone C was dissolved in ether and extracted twice with 21% sodium bisulfite solution. Evaporation of the ether yielded 2.35 grams of material. The material was dissolved in boiling water and, on cooling, 1.7 grams of light colored crystals were obtained that melted at 110-114°. Crystals obtained after decolorizing by boiling in a mixture of water and carbon black melted at 112-114° and gave no depression in a mixed melting point with acetovanillone. The mother liquor from the first crystallization was combined with the bisulfite solution. The solution was acidified with sulfuric acid, boiled, and then extracted with ether. Evaporation of the ether yielded 1.8 grams of crystalline material. Crystallization from boiling petroleum ether gave a crude material melting at 64-74°. In order to affect further purification, the crude material was dissolved in 10% sodium hydroxide solution and saturated with sulfur dioxide, after which it was extracted with ether. Evaporation of the ether solution yielded 0.2 gram of crystals melting at 104-111°. (This material was recrystallized from water and identified as acetovanillone by a mixed melting point.) The bisulfite solution was acidified, boiled, and then extracted with ether. Evaporation of the ether gave 1.5

grams of material melting at 71-77°. Recrystallization from petroleum ether yielded crystals melting at 78-80° which did not give a melting point depression when mixed with vanillin.

Zone D yielded a dark viscous oil which appeared to be resinous. It was obtained in very small yield and was not characterized.

4'-HYDROXY-3'-METHOXYFLAVANONE

4'-Hydroxy-3'-methoxyflavanone [prepared by B. Sen (14)] (3.0 grams) was cooked in 60 ml. cooking liquor B for five hours at 160°. The product was isolated in the regular manner. The yield was 2.5 grams of crystalline material. The product was yellow colored and had the odor of o-hydroxyacetophenone.

A benzene solution of the product (2.5 grams) was chromatographed on a No. 3 column, using two column lengths of 200:1 benzene-ethanol solution as a developer. The chromatogram obtained was identical with the chromatogram of the 2',4-dihydroxy-3-methoxychalcone reaction product. However, the separation of zones was modified because past experiences indicated a more suitable technique. The results of the chromatographic separation are given below.

Zone	Streaking Results	Recovered Material g.	%
A	Green ferric chloride	0.10	4.0
B	Orange 2,4-D.P.H. Yellow colored bands	1.45	58.0
C	Violet ferric chloride Reduced permanganate	0.81	32.4
		2.36	94.4

The dark crystalline material from zone A apparently was protocatechualdehyde. The green ferric chloride test and the position of the zone in the chromatogram were the same as those of protocatechualdehyde isolated in the 2',4-dihydroxy-3-methoxychalcone cook.

A paper chromatogram of the material from zone B was run, with vanillin, 2',4-dihydroxy-3-methoxychalcone, and 4'-hydroxy-3'-methoxyflavanone as reference substances. Butanol saturated with 2% ammonia was used as a developer. The chromatogram indicated that zone B contained mainly vanillin and a small amount of the chalcone; the flavanone was not detected.

The crystalline product from zone B was dissolved in 10% sodium hydroxide solution and saturated with sulfur dioxide. A yellow oil separated and was extracted with ether. Evaporation of the ether yielded approximately 0.05 gram of yellow material. It was crystallized from dilute ethanol to give needles which melted at 125-127° and did not depress a mixed melting point with 2',4-dihydroxy-3-methoxychalcone. The bisulfite solution was acidified with sulfuric acid, boiled, and extracted with

ether. The ether extract yielded 1.3 grams of crystals melting at 78-81°. Recrystallization from petroleum ether gave crystals that melted at 79-81° and gave no depression in a mixed melting point with vanillin.

The oil from zone C was converted to an acetate by reacting with acetic anhydride in pyridine overnight. The yield was 0.70 gram of white material melting at 81-86°. The material was recrystallized from dilute ethanol to give a product melting at 86-88°. A mixed melting point with o-acetoxyacetophenone gave no depression.

2-VANILLYLIDENE-3-COUMARANONE

2-Vanillylidene-3-coumaranone (4.0 grams) was cooked in 80 ml. of cooking liquor B for five hours at 160°. The resulting liquor contained an appreciable amount of finely divided precipitate. By using the general procedure, approximately 3.1 grams of oil were obtained as a product from the liquor. When the autoclave was being cleaned, a considerable amount of solid material was found in the relief line. This material was removed by dissolving with acetone. Evaporation of the acetone yielded 0.3 gram of solid material that was insoluble in water and dilute alkali. The material contained no ash or sulfur. It appeared to decompose at 150-170°.

The main oily product (3.1 grams) was chromatographed on a No. 3 column, using 150:1 benzene-ethanol solution as a developer. The results of the chromatographic separation are given below.

Zone	Streaking Results	Material Recovered g.	%
A	Green ferric chloride	0.23	7.4
B	Yellow colored band Orange 2,4-D.P.H.	2.22	71.6
C	Reduced permanganate	0.52	16.8
		2.97	95.8

A paper chromatogram was run with the products from zones A, B, and C, with vanillin, protocatechualdehyde, and 2-vanillylidene-3-coumaranone as reference substances. The chromatogram was developed with butanol saturated with 2% aqueous ammonia, and indicated that zone A contained approximately equal amounts of protocatechualdehyde and an unknown material which moved with the leading edge of the butanol solution. Zone B contained mainly vanillin. A small amount of 2-vanillylidene-3-coumaranone was also indicated, together with a colored material that moved with the leading edge of the chromatogram. The material from zone C moved as a single spot with the leading edge.

The material from zone C, an oily solid, was boiled in methyl alcohol and filtered. Approximately 0.1 gram of methanol-insoluble product was obtained which melted at 238-240° with decomposition. The material was dissolved in hot acetone and diluted with water. On cooling, a flocculent material formed (30 mg.) which melted at 240-241.5° with decomposition. This product did not contain sulfur and was insoluble in dilute alkali. The methanol solution was evaporated to yield an oil. The oil was dissolved in hot acetone and diluted with water. Approximately 0.2 gram of

solid material was obtained. The material had no definite melting point, but seemed to decompose at 300-310°. The product did not contain sulfur and was insoluble in alkali. Further characterization of the material from zone C was not accomplished.

The crystalline material from zone B was dissolved in 10% sodium hydroxide and saturated with sulfur dioxide. The oily material which separated was extracted with ether. Evaporation of the ether yielded 1.0 gram of an oily solid. The bisulfite solution was acidified, boiled, and extracted with ether. The ether extract gave 1.2 grams of crystals melting at 68-75°. Recrystallization from petroleum ether yielded crystals that melted at 78-80° and gave no depression in a mixed melting point with vanillin.

The bisulfite-insoluble material (1.0 gram) from zone B was combined with the dark product from zone A (0.2 gram) and rechromatographed on a No. 3 column, using four column lengths of 150:1 benzene-ethanol solution as a developer. The results of the chromatogram are given below.

Zone	Streaking Results	Material Recovered g.	%
A'	Dark band at top of column	nil	- -
B'	Red colored band	nil	- -
C'	Green ferric chloride	0.20	16.7
D'	Orange 2,4-D.P.H.	0.40	33.3
E'	Yellow colored band	0.10	8.3
F'	Effluent	0.30	25.0
		1.00	83.3

Zone C' yielded a crystalline material that melted at 140-148°. It was recrystallized from benzene to give a light colored product melting at 145-150°. A mixed melting point with protocatechualdehyde (m.p. 151-153°) was 146-150°.

The product from zone D' was recrystallized from petroleum ether to yield crystals that melted at 77-80° and gave no depression in a mixed melting point with vanillin.

The oily solid from zone E' was washed with a solution of methanol and chloroform; the crystalline material melted at 196-200°. A mixed melting point with 2-vanillylidene-3-coumaranone (m.p. 201-202°) was 196-201°.

A viscous oil was obtained from the effluent that was soluble in methanol, chloroform, and benzene and insoluble in alkali. When boiled in a solution of 4:1 petroleum ether and chloroform, a black tarry residue formed. On cooling the mother solution, an oil separated. A test for sulfur was negative.

VANILLIN

Vanillin (4.0 grams) was cooked in 100 ml. of cooking liquor B for five hours at 160°. The regular procedure was employed to isolate 3.54 grams of product.

The product (3.0 grams) was chromatographed on a No. 3 column, using

two column lengths of 100:1 benzene-ethanol solution as a developer. The results of the chromatogram are given below.

Zone	Streaking Results	Material Recovered g.	%
A	Green ferric chloride Reddish brown 2,4-D.P.H.	0.10	3.3
B	Violet ferric chloride Orange 2,4-D.P.H.	2.63	87.7
		2.73	91.0

Most of the product from zone A dissolved in boiling benzene; when the hot solution was filtered and cooled, a light colored product crystallized and melted at 149.5-151.5°. No depression occurred in a mixed melting point with an authentic sample of protocatechualdehyde (m.p. 151-152°).

The light colored crystalline material from zone B melted at 77-81°. It melted at 79-81° after one crystallization from petroleum ether and gave no depression in a mixed melting point with vanillin.

ω-(4-ACETYL-2-METHOXYPHENOXY)ACETOVANILLONE

The customary cooking liquor B was not alkaline enough to dissolve ω-(4-acetyl-2-methoxyphenoxy)acetovanillone, even when heated. Therefore, the cooking liquor was modified for this cook.

ω-(4-Acetyl-2-methoxyphenoxy)acetovanillone (3.0 grams) was cooked with a solution containing 160 ml. of liquor B and 60 ml. of 5% sodium hydroxide solution for five hours at 160°. Although the compound was not

soluble prior to cooking, the reaction product was completely soluble. Using the general procedure, 2.3 grams of yellow crystalline material were obtained as a product. The product melted at 95-109°.

A paper chromatogram was run with the product, together with acetovanillone and ω-(4-acetyl-2-methoxyphenoxy)acetovanillone as reference substances. The chromatogram was developed with butanol saturated with 2% aqueous ammonia and indicated that the product was almost entirely acetovanillone. No ω-(4-acetyl-2-methoxyphenoxy)acetovanillone was detected in the product.

The product (2.3 grams) was chromatographed on a No. 3 column, using two column lengths of 25:1 petroleum ether (60-110°) and ethanol solution as a developer. The results of the chromatogram are given below.

Zone	Streaking Results	Material Recovered g.	%
A	Yellow colored band	0.27	11.7
B	Both green and violet ferric chloride color	1.95	84.7
		2.22	96.4

The material from zone A was a dark, partially crystallized oil. It could not be crystallized from ethanol or benzene solution.

Zone B yielded a crystalline product that melted at 103-112°. The material (1.95 grams) was rechromatographed on a No. 3 column, using two

column lengths of 100:1 benzene-ethanol solution as a developer. The results of the separation are given below.

Zone	Streaking Results	Material Recovered g.	%
A'	Green ferric chloride Orange 2,4-D.P.H.	0.05	2.5
B'	Orange 2,4-D.P.H.	1.87	96.0
		1.92	98.5

The colorless oil obtained from zone A' was evidently demethylated material because of its position on the column and the green ferric chloride color. The material formed sticky crystals when treated with benzene. [Demethylated acetovanillone (4-acetopyrocatechol) can be crystallized from benzene.] The product could not be obtained in a pure crystalline state because of the insufficient quantity available for recrystallization.

Zone B' yielded a light colored crystalline product that melted at 106-112°. Approximately 0.5 gram of the material was boiled in water with decolorizing carbon. After filtering and cooling, white crystals (0.4 gram) formed. The crystals melted at 110-113° and gave no depression in a mixed melting point with acetovanillone.

Because only 2.3 grams of product (77% of the starting material) were recovered, it was evident that considerable product remained in the liquor. The liquor was therefore acidified with dilute sulfuric acid and extracted twice with ether. The yellow colored ether extract was dried over sodium sulfate and evaporated to yield a dark oil mixed with a white solid. The

oil was dissolved in acetone and filtered. The white solid, which was insoluble in acetone, burned with a blue flame, and the characteristic odor of burning sulfur was detected. The filtrate was combined with the material from zone A of the first chromatogram and shaken with mercury to remove any free sulfur. The solution was filtered and then evaporated to yield 0.70 gram of a dark viscous oil.

The viscous oil (0.70 gram) was chromatographed on a No. 2 column using 100:1 benzene-ethanol solution as a developer. The results of the chromatographic separation are given below.

Zone	Streaking Results	Material Recovered g.	Material Recovered %
C	Dark band at top of column	0.10	14.3
D	Dark green ferric chloride	0.15	21.4
E	Red ferric chloride	0.27	38.6
F	Blue ferric chloride	0.11	15.7
		0.63	90.0

All the materials from the different zones, except zone F, were dark oils. Zone F yielded light colored crystals melting at 78-103°.

A paper chromatogram was run with the materials from zones D, E, and F, with acetovanillone, guaiacol, and creosol as reference substances. The chromatogram indicated that zone F contained mainly acetovanillone. Both zones D and E contained a material having the same R_f value as ω-(4-acetyl-2-methoxyphenoxy)acetovanillone. The chromatogram indicated that zones D and E contained complicated mixtures of unknown substances.

1-(4-HYDROXY-3-METHOXYPHENYL)-1-PROPANOL

Sodium Hydrosulfide Cooks at 160°

Several cooks were carried out with 1-(4-hydroxy-3-methoxyphenyl)-1-propanol at 160°, using both liquors A and B. In the cooks with liquor A, a residue which contained ash was formed in the autoclave. However, on dissolving the residue in ethanol (it was insoluble in water) and acidifying, a product was obtained that was similar to the material extracted from the liquor. When liquor B was employed, a clear solution resulted after the cook.

Whether liquor A or B was used, the products were essentially the same. The products were sticky oils that had a strong garlic odor. When exposed to air for a considerable time, the oils darkened and slowly lost their strong odor. Qualitative sodium fusion tests failed to indicate the presence of sulfur.

Various solvents were used in attempts to crystallize the oily product but no crystalline material could be obtained. The oil was very soluble in ethanol, chloroform, ether, benzene, and acetone. It was insoluble in petroleum ether. When a chloroform solution of the oil was slowly poured into petroleum ether, a flocculent precipitate formed. The precipitate (when filtered and dried) was an amorphous solid that softened but did not melt. The solid could be reconverted to an oil by evaporating an ether solution of the solid.

Chromatographic techniques failed to accomplish a separation of the

mixture. Both benzene-ethanol and petroleum ether-alcohol solutions were used as developers. In every case, diffuse columns were obtained with no distinct zones. A paper chromatogram was run with the product and 1-(4-hydroxy-3-methoxyphenyl)-1-propanol as a reference substance. The product moved as a single spot with the leading edge of the developer. The presence of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol in the product could not be detected. Several paper chromatograms were run using paper saturated with different buffered solutions. Leopold (29) has used this technique with much success in separating different phenolic materials. The developing solutions consisted of either butanol or petroleum ether saturated with water. No separations of the product could be affected by using buffered paper.

On converting the oily product to an acetate, no change was detected. The acetate was a sticky oil that could not be crystallized.

A lead salt of the product was obtained by treating an alcoholic solution of the oil with lead acetate. A yellow precipitate formed that was insoluble in water, alcohol, acetone, and ether. By washing the precipitate with dilute acetic acid, a light colored material was obtained which was free of lead and soluble in organic solvents.

Characterization of the Reaction Product

1-(4-Hydroxy-3-methoxyphenyl)-1-propanol (10.0 grams) was cooked in 100 ml. of liquor B for five hours at 160°. By using the general procedure, 10.2 grams of colorless oil were obtained as a product.

Approximately five grams of the oil were distilled at 0.3 mm. pressure. The oil distilled over a range of 100-260° with no apparent interruptions in the rate of distillation. Approximately 80% of the material did not distill. On cooling, the residue solidified to form a glass. The distillate remained as an oil. The molecular weights (Rast) of the residue and of the 150-260° distillate were found to be 715 and 215, respectively.

A portion of the original oil was dissolved in ether and shaken with mercury. The black precipitate that formed was filtered and the filtrate was again shaken with mercury. The second treatment with mercury caused only slight formation of the black precipitate. The filtered ether solution was evaporated to yield a viscous oil.

Analysis of the oil: C, 68.04%; H, 7.78%; S, 0.4%; Rast molecular weight, 360.

Reaction of Mercury with Disulfides

Although mercury was found to react very readily with free sulfur, its reactivity with organically bound sulfur was uncertain. A reaction was carried out with mercury and bisbenzyl disulfide in order to establish the suitability of removing free sulfur with mercury.

Mercury was shaken with 1.0 gram of bisbenzyl disulfide in ether for two hours. The black precipitate that formed was filtered. Evaporation of the ether solution yielded white crystals melting at 67-70°. The crystals were dissolved in ether and again shaken with mercury for 24 hours. Repeating the filtration and evaporation gave 0.87 gram of white crystals

melting at 67-70°. A mixed melting point with bisbenzyl disulfide (m.p. 70-71°) gave no depression. The black precipitate again formed when an ether solution of the crystals was shaken with mercury for the third time.

The above reaction was repeated using a few mg. of bis[1-(4-hydroxy-3-methoxyphenyl)-1-propyl] disulfide in an ether solution. The black precipitate formed as before. No attempt was made to recover the unreacted disulfide.

Neutral Sulfide Cook of 1-(4-Hydroxy-3-methoxyphenyl)-1-propanol

One gram of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol was sealed in a glass tube containing 40 ml. of buffered cooking liquor (pH 6.8) and heated for 72 hours at 100°. The cooking liquor (120 ml., containing 3.26 grams of sodium sulfide, 14.8 ml. of propionic acid, and 4.96 grams of potassium hydroxide) was the same as that described by Enkvist (16). After cooling, the aqueous layer was decanted and the residual oil was dissolved in ether. The ether solution was washed with sodium bicarbonate solution, dried over sodium sulfate, and evaporated to yield approximately 0.7 gram of oil. A benzene solution of the oily product (0.7 gram) was chromatographed on a No. 3 column, using two column lengths of 250:1 benzene-ethanol solution as a developer. Two distinct zones were detected, the upper zone A containing 0.45 gram of oil and the lower zone B containing 0.2 gram. The oil from zone B had the odor of isoeugenol and the position of zone B on the chromatogram corresponded to that of isoeuganol.

A 3,5-dinitrobenzoate of the material from zone B was prepared by refluxing the oil with pyridine and 3,5-dinitrobenzoyl chloride for 30

minutes. A yellow solid formed when the solution was poured into ice water. Recrystallizing the product three times from butanol yielded crystals melting at 156.5-157.5°. The crystals gave no depression in a mixed melting point with authentic isoeugenol 3,5-dinitrobenzoate (m.p. 156-158°).

The oily material from zone A was similar to the product from the regular cook at 160°. It could not be crystallized nor purified by chromatography.

Sodium Hydrosulfide Cook at 100°

Three grams of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol were cooked in 60 ml. of liquor B for six hours at 100°. Following the general procedure, 2.7 grams of oil were obtained as a product. The oil had the typical strong garlic odor. The material was similar to the reaction products obtained from the cooks at 160° in that it could not be crystallized or separated by chromatography.

The oily material was treated with mercury three times to remove any free sulfur and was then analyzed for sulfur.

Analysis: S, 5.2%.

Sodium Hydrosulfide Cook at 85°

Two grams of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol were cooked in 40 ml. of liquor B for 16 hours at 85°. The product was isolated by using the general procedure; the yield was 1.7 grams of oil. The oil was treated with mercury to remove any free sulfur and was then analyzed for sulfur.

Analysis: S, 5.3%; Rast molecular weight, 290

Two-Stage Sodium Hydrosulfide Cook

Two grams of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol were cooked in 40 ml. liquor B for 16 hours at 85°. The solution was then transferred to the autoclave and cooked at 160° for two hours. After cooling overnight, the liquor was neutralized with dilute sulfuric acid. The precipitate that formed was filtered and dried. The yield was 1.7 grams of solid material.

The product was dissolved in 0.2 N sodium hydroxide solution, filtered, and precipitated by neutralizing with 0.1 N hydrochloric acid. The light colored solid was filtered and dried. It was then dissolved in a small amount of chloroform and precipitated into petroleum ether (60-110°). The mixture was centrifuged and the organic solution was decanted. The solid when dried was light colored. Drying under a vacuum at 76° caused the product to darken somewhat.

Analysis: S, 0.4%; Rast molecular weight, 880

Reactions with Sodium Hydrosulfide at Room Temperature

Two grams of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol were stirred in 50 ml. of liquor A. Since approximately only 0.2 gram of the compound was soluble in 25 ml. of the liquor at room temperature, the mixture was heated to 90° to effect solution. An experiment described later indicated that no reaction occurred during the dissolving step. The solution was filtered to remove a slight amount of oil and cooled. On standing overnight, a white solid separated. The solution was filtered and more white material precipitated during a two-day period. The solution was filtered and the precipitate was washed with water and ether. Approximately 0.2

gram of solid was obtained. It contained ash and gave a test for sulfur. The material darkened and melted at 205-210°. It was dissolved in absolute ethanol and acidified with 0.1 N hydrochloric acid. The solution was diluted with water and extracted with ether. Evaporation of the ether yielded a white solid melting at 107-109°. Recrystallizing from dilute ethanol gave a material that melted at 115-116°. Analysis of the product corresponded to that of bis[1-(4-hydroxy-3-methoxyphenyl)-1-propyl] disulfide.

Analysis: Calculated for $C_{20}H_{26}O_4S_2$: C, 60.90%; H, 6.65%; S, 16.3%; mol. wt., 394. Found: C, 61.06%; H, 6.67%; S, 16.5%; mol. wt. (Rast), 375.

The original aqueous filtrate was saturated with hydrogen sulfide and sodium chloride. A white solid separated (0.90 gram) that melted at 80-82°. A mixed melting point with 1-(4-hydroxy-3-methoxyphenyl)-1-propanol gave no depression. The solution then was extracted with ether. Evaporation of the ether yielded 0.4 gram of a white solid. Recrystallization of the material from carbon tetrachloride gave crystals melting at 82-84°. No depression was noted in a mixed melting point with 1-(4-hydroxy-3-methoxyphenyl)-1-propanol.

Extended Reaction With Sodium Hydrosulfide at Room Temperature

The reaction at room temperature was repeated with 2.5 grams of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol, using the procedure described above. A white flocculent solid began to form two hours after the solution was filtered and cooled. The solution was allowed to stand for three weeks in

a stoppered flask. Precipitation appeared to cease after the fourth day and the solution turned to a deep yellow color. The precipitate was filtered to yield 0.4 gram of white solid. The product was dissolved in warm ethanol and 0.1 N hydrochloric acid was added until the solution just became cloudy. On cooling crystals formed. The yield was 0.26 gram of material melting at 114.5-117°. The crystals gave no depression in a mixed melting point with bis[1-(4-hydroxy-3-methoxyphenyl)-1-propyl] disulfide.

The mother liquor was saturated with hydrogen sulfide and extracted with ether. Evaporation of the ether yielded 2.2 grams of oil that partially crystallized on standing. The material could not be recrystallized from alcohol or benzene. Approximately 1.5 grams of the oily solid were dissolved in acetic acid and a 1% solution of mercuric acetate in acetic acid was added. A white precipitate formed immediately. The precipitate was filtered (0.15 gram) and the mother liquor was extracted with ether. The ether extract was washed with water and sodium bicarbonate solution, dried over sodium sulfate, and evaporated. Approximately 1.2 grams of an oily solid was obtained. Recrystallizing from dilute ethanol yielded 0.55 gram of crystals melting at 168-177°. A second crystallization gave a material that melted at 179-180° and did not give a depression in a mixed melting point with diisoeugenol.

Analysis: Calculated for diisoeugenol, $C_{20}H_{24}O_4$: MeO, 18.9%. Found: MeO, 18.9%.

The white precipitate which formed in the treatment with mercuric acetate contained sulfur and mercury. It reduced iodine when a suspension was heated in acetic acid. The material did not contain methoxyl groups. It was evidently an inorganic salt of mercury.

One gram of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol was dissolved in acetic acid and treated with 1% mercuric acetate in acetic acid. No precipitate formed. The solution was extracted with ether. The ether extract was washed with water and sodium bicarbonate solution, dried over sodium sulfate, and evaporated to yield an oil. The oil could not be crystallized from dilute ethanol. A paper chromatogram was run with the oil and diisoeugenol as a reference substance. No diisoeugenol could be detected in the oil.

Dissolving Experiment

An experiment was carried out to determine whether the disulfide was formed during the dissolving step.

One gram of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol was dissolved in 25 ml. of a solution containing 1.76 grams of sodium hydroxide and heated to 90°. Hydrogen sulfide was introduced until a slight turbidity formed. On cooling, white crystals separated. The material was filtered to yield 0.4 gram of crystals that melted at 84.5-85° and gave no depression in a mixed melting point with 1-(4-hydroxy-3-methoxyphenyl)-1-propanol. The mother liquor was extracted with ether. Evaporation of the ether yielded 0.5 gram of material melting at 83-84°.

DISCUSSION

Model compounds containing four types of functional groups were studied in the sodium hydrosulfide cooking experiments. The functional groups included the carbonyl group, the conjugated double bond, the ether linkage, and the aliphatic hydroxyl group. The products identified from the different model compounds are listed in Table II.

Compounds containing the carbonyl group did not react to form sulfur derivatives. Propiovanillone was very resistant to the action of sodium hydrosulfide. After cooking four hours at 160°, approximately 80% of the propiovanillone was recovered unchanged. A small amount of 4-propionylpyrocatechol (demethylated propiovanillone) was also obtained as a product. Cooking propiovanillone for 30 hours at 160° increased the demethylation (15-20% yield of 4-propionylpyrocatechol), but 65-70% of the propiovanillone was recovered unchanged.

The action of sodium hydrosulfide on a conjugated double bond was studied by cooking substituted chalcones. The chalcones were 2',4-dihydroxy-3-methoxychalcone and 4,4'-dihydroxy-3,3'-dimethoxychalcone. The reaction of another model compound containing a conjugated double bond, 2-vanillylidene-3-coumaranone, was also studied.

The alkaline sulfide reagent appeared to have the same effect upon all α,β-unsaturated ketones studied. In each case, a reverse aldol occurred and the corresponding ketones and aldehydes were formed.

TABLE II

MODEL COMPOUNDS AND THEIR PRODUCTS

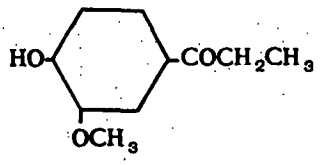
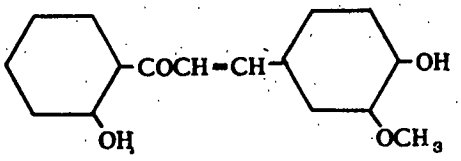
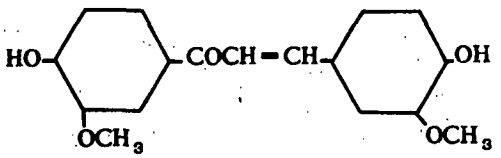
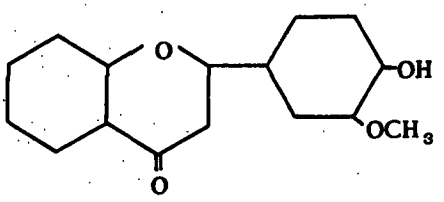
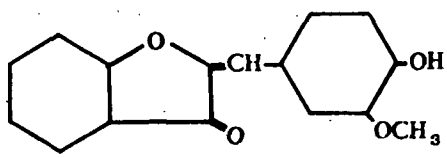
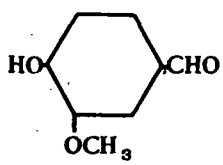
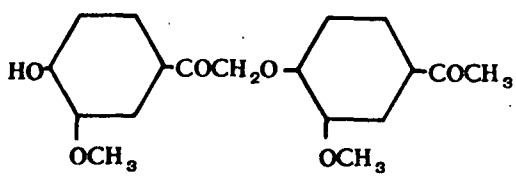
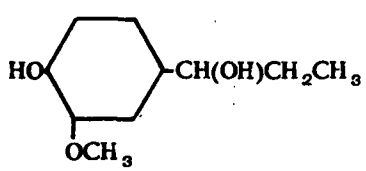
Model Compounds	Products
Propiovanillone 	Propiovanillone 4-Propionylpyrocatechol
2',4-Dihydroxy-3-methoxychalcone 	Vanillin *o*-Hydroxyacetophenone Protocatechualdehyde 2',4-Dihydroxy-3-methoxychalcone
4,4'-Dihydroxy-3,3'-dimethoxychalcone 	Vanillin Acetovanillone 4,4'-Dihydroxy-3,3'-dimethoxychalcone
4'-Hydroxy-3'-methoxyflavanone 	Vanillin *o*-Hydroxyacetophenone 2',4-Dihydroxy-3-methoxychalcone

TABLE II (Continued)

MODEL COMPOUNDS AND THEIR PRODUCTS

Model Compounds	Products
2-Vanillylidene-3-coumaranone 	Vanillin Protocatehualdehyde 2-Vanillylidene-3-coumaranone
Vanillin 	Vanillin Protocatechualdehyde
ω-(4-Acetyl-2-methoxyphenoxy)acetovanillone 	Acetovanillone
1-(4-Hydroxy-3-methoxyphenyl)-1-propanol 	Bis [1-(4-hydroxy-3-methoxyphenyl)-1-propyl] disulfide Isoeugenol Diisoeugenol

Four products were isolated from the 2',4-dihydroxy-3-methoxychalcone cook to account for over 90% of the starting material. Vanillin and o-hydroxyacetophenone were the main products, and small amounts of the unreacted chalcone and protocatechualdehyde (demethylated vanillin) were obtained.

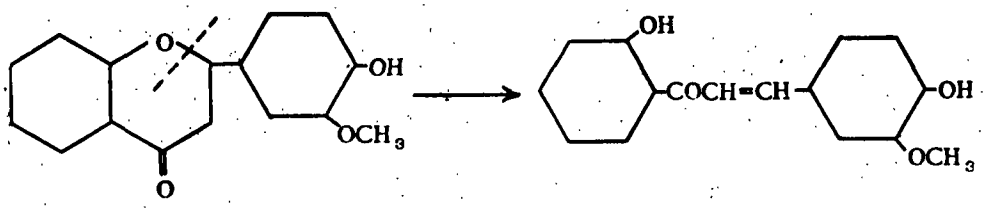
Vanillin and acetovanillone were the main products obtained from cooking 4,4'-dihydroxy-3,3'-dimethoxychalcone. These products accounted for over 75% of the starting material. A small quantity of the unreacted chalcone was identified, and demethylated products were indicated by chromatograms, although none was isolated and identified as such.

The reaction products of 2-vanillylidene-3-coumaranone were not completely accounted for. The isolation of protocatechualdehyde and approximately 80% of the theoretical amount of vanillin indicated that a reverse aldol reaction occurred. However, coumaranone, which would be the other component of the reverse aldol reaction, was not obtained. Instead, mixtures of high melting solids and viscous oily products were obtained. Evidently, coumaranone underwent autocondensation under the alkaline conditions. The fact that these complex products were not soluble in alkali indicated that the heterocyclic ring was not broken. (Otherwise a free phenolic group would have been liberated.) The possibility that coumaranone formed condensation products was indicated by studies of Fries and Pfaffendorf (30). They found that coumaranone could be condensed under different alkaline conditions to form a variety of products; some of the products were identified as dimers but other products were reported as high melting solids and viscous oils.

Protocatechualdehyde was isolated from each of the cooks in which vanillin was a product. In previous investigations of lignin degradation products where vanillin was isolated, the presence of protocatechualdehyde was not reported. This suggested the possibility that demethylation occurred prior to the formation of vanillin in the reverse aldol reaction. However, the fact that protocatechualdehyde (2-3% yield) was isolated from the vanillin cook proves that vanillin itself can be demethylated under the cooking conditions used. Approximately 75% of the vanillin was recovered unchanged. The high yield of vanillin indicated a marked difference in the cooking liquor employed in this investigation and that used by Enkvist (16). Enkvist cooked vanillin with a sodium hydrosulfide solution (pH 8.1) at 160° for five hours and recovered only 15% of the vanillin. The other products were amorphous and contained sulfur.

Recently, Jayne (31) has carried out an alkaline nitrobenzene oxidation of vanillin at 160°; among other products, a small amount of protocatechualdehyde was indicated by paper and column chromatograms. This implies that demethylation is not specific to the action of the alkaline sulfide reagent. Indeed, it seems likely that demethylated products were formed in the previous investigations but these products were not isolated and identified because suitable techniques were not available for isolating such small amounts of material. It is felt that when the more sensitive techniques, such as chromatography, are employed to study lignin degradation products, the isolation of demethylated products will become more common.

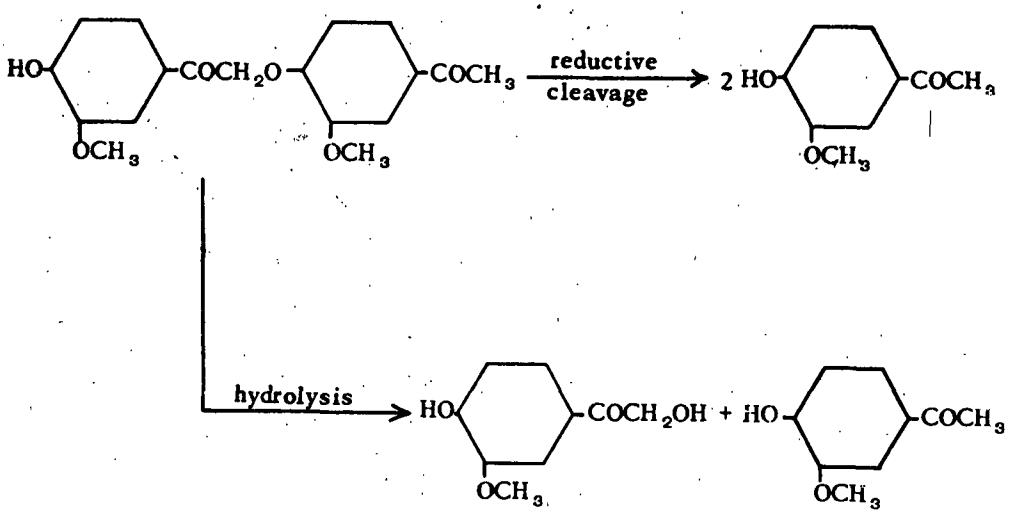
The model compound 4'-hydroxy-3-methoxyflavanone contains a "masked" conjugated double bond. Splitting the heterocyclic ring could cause the formation of 2',4-dihydroxy-3-methoxychalcone. Evidently, when 4'-hydroxy-3'-methoxyflavanone was subjected to the action of the



sodium hydrosulfide cook, the initial reaction involved the formation of the corresponding chalcone. The products of the cook were identical with those obtained from cooking 2',4-dihydroxy-3-methoxychalcone--i.e., vanillin and o-hydroxyacetophenone were the main products and small amounts of protocatechualdehyde and 2',4-dihydroxy-3-methoxychalcone were obtained. If unreacted 4'-hydroxy-3'-methoxyflavanone was present in the product, it was in such a small quantity that it could not be detected by paper chromatograms.

The action of the alkaline sulfide reagent on an ether linkage, other than the methoxyl group, was studied by cooking ω-(4-acetyl-2-methoxyphenoxy)acetovanillone. Hydrolysis of the ether linkage should form two products, ω-hydroxyacetovanillone and acetovanillone. If reductive cleavage took place, only acetovanillone should be formed. A study of the reaction products indicated that the ether linkage was split by a reducing reaction; acetovanillone was isolated in sufficient quantity to account for approximately 70% of the starting material. A mixture of other products (about 20%) was also obtained. Chromatograms indicated that the mixture contained four or five different materials of which the starting material was the chief component.

A small amount of demethylated material, possibly 4-acetylpyrocatechol, was also indicated by chromatograms.



The reactivity of the aliphatic hydroxyl group with sodium hydrosulfide was studied by cooking 1-(4-hydroxy-3-methoxyphenyl)-1-propanol. The results indicated that the compound was very reactive toward sodium hydrosulfide. Cooking at 160° produced a product that could not be identified. In Table III, the elementary analysis of the reaction product is compared with the elementary composition of the starting material and that of isoeugenol (or its polymerization products).

TABLE III

CHARACTERIZATION OF 160° REACTION PRODUCT

	Model Compound	Reaction Product	Isoeugenol, diisoeugenol or polymeric derivatives
C, %	65.8	68.0	73.1
H, %	7.7	7.8	7.3
O (by difference), %	26.5	23.8[1]	19.4
Mol. wt.	182	360[2]	- -

1. Product also contained 0.4% sulfur
2. Rast molecular weight

The molecular weight data from Table III indicated that 1-(4-hydroxy-3-methoxyphenyl)-1-propanol polymerized during the cook. The loss of oxygen and the increase in the carbon content pointed to the possibility that dehydration occurred. The case with which 1-(4-hydroxy-3-methoxyphenyl)-1-propanol was dehydrated was shown by the formation of isoeugenol on distillation. Attempts to distill the reaction product failed to produce a pure product. A fraction distilling from 150-260° at 0.3 mm. pressure had a molecular weight (Rast) of 215. The molecular weight of the distillation residue was 715. Evidently the polymerized product was partially fractionated by distillation. Additional polymerization could have occurred during the distillation. Because of the apparent complexity of the reaction during cooking, an extended study of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol under different reaction conditions was carried out.

1-(4-Hydroxy-3-methoxyphenyl)-1-propanol reacted with sodium hydrosulfide at room temperature to form bis[1-(4-hydroxy-3-methoxyphenyl)-1-propyl] disulfide. The reaction took place in aqueous or alcoholic solutions. It was noted that the formation of the disulfide depended upon the presence of air. Evidently the mercaptan was formed as an intermediate. The oxidation of mercaptans in alkaline solution by air is a well-known reaction.

In addition to the disulfide, an oily product was also obtained from the room temperature reaction. When the oily material was treated with mercuric acetate in acetic acid, diisoeugenol was isolated. Diisoeugenol could not be obtained by treating 1-(4-hydroxy-3-methoxyphenyl)-

1-propanol with mercuric acetate. The mechanism for the formation of diisoeugenol could not be determined. However, the formation of diisoeugenol indicates that the side chain may be involved in the polymerizing reactions of the model compound.

When 1-(4-hydroxy-3-methoxyphenyl)-1-propanol was cooked with sodium hydrosulfide at 100° for six hours, a product was obtained that contained 5.2% sulfur. The product was treated with mercury prior to analysis to insure the complete removal of free sulfur. Besides removing free sulfur, mercury was shown to react slowly with chemically bound sulfur. Therefore, the sulfur contents of the products treated with mercury may be slightly low.

Because the regular 160° cooking product contained a very slight amount of sulfur, it seemed likely that sulfur was removed from the product at the high temperature. This was further shown by a comparison of two reaction products. The first product was formed by reacting the model compound with sodium hydrosulfide at 85° for 16 hours. The product contained 5.2% sulfur and its molecular weight (Rast) was 290. The second product was obtained from a two-stage reaction; the first stage involved reacting for 16 hours at 85° and the second stage involved reacting for two hours at 160°. The sulfur content of the second product was 0.4% and its molecular weight (Rast) was 880. A comparison of the products from the two experiments indicated that the high temperature not only decomposed the sulfur compound but also caused polymerization.

1-(4-Hydroxy-3-methoxyphenyl)-1-propanol was also reacted with a neutral sulfide solution at 100° for 72 hours. Enkvist (16) obtained

vanillyl disulfide from vanillyl alcohol under such conditions. Isoeugenol (20% yield) was the only product identified from the reaction of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol. Evidently, heating the undissolved model compound was more conducive to dehydration than to the formation of a sulfur derivative.

Although the pH of the cooking liquor employed by Enkvist (16) was much lower than that used in the present investigation, two similarities were noted in the reactions of the hydroxyl group. Under mild conditions both vanillyl alcohol and 1-(4-hydroxy-3-methoxyphenyl)-1-propanol reacted to form disulfides and, at 160°, the disulfides were not obtained. In fact, nonsulfur-containing products were obtained from the 160° cooks; vanillin was a product of vanillyl alcohol and an unidentified nonsulfur-containing polymer was a product of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol.

It would be extremely unwise to interpret all the reactions of lignin during the kraft cook on the basis of reactions of a few model compounds. However, the results of the model compound cooking experiments do point out certain reactive groups as well as nonreactive groups. For example, the results indicate the improbability of a carbonyl group reacting to form a sulfur derivative during the kraft cook. Although α, β-unsaturated ketones are readily sulfonated, it is doubtful whether a similar reaction can take place with the sulfide ion in the kraft cook. A reverse aldol reaction hydrolyzes such groups before an addition reaction is possible.

A similarity was noted in the room temperature reactions of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol and of native lignin. Both materials reacted to form sulfur derivatives. Indeed, of the different functional groups studied, only the hydroxyl group was noted to react with the alkaline sulfide ion to form a sulfur derivative. The instability of the sulfur derivatives at higher temperatures is not wholly different from that of thiolignin. Thus, Ahlm (6) found that the sulfur in thiolignin was readily split off in the presence of alkali. Approximately one half of the sulfur was lost when Ahlm methylated thiolignin with dimethyl sulfate and sodium hydroxide. These results definitely point to the possibility of hydroxyl groups in lignin being responsible for the introduction of sulfur during the kraft cook.

An interesting observation with respect to kraft odors was noted in the model compound cooks. Although all cooks had a slight kraft odor, only the 1-(4-hydroxy-3-methoxyphenyl)-1-propanol cook had the strong garlic odor. In view of the fact that demethylation occurred in the other cooks, the mild odors of the cooks indicate that methyl mercaptan or methyl disulfide was not formed during demethylation reactions. There has been considerable speculation on this subject in the past, and many investigators have ascribed the formation of kraft odors (methyl mercaptan, etc.) to the demethylation reaction of lignin. If the ether cleavage of ω-(4-acetyl-2-methoxyphenoxy)acetovanillone is typical of the kraft cook, then demethylation of lignin should produce methane rather than methyl mercaptan. A hydrolytic cleavage of the methoxyl group would cause the formation of methyl alcohol. The mechanism of the demethylation was not established in this investigation.

SUMMARY AND CONCLUSIONS

1. A number of model compounds have been synthesized and subjected to the sodium hydrosulfide cook. The model compounds contained four types of functional groups: the carbonyl group, the conjugated double bond, the ether linkage, and the hydroxyl group.

2. Only the model compound containing a hydroxyl group reacted with the alkaline sulfide ion to form a sulfur derivative. At room temperature, 1-(4-hydroxy-3-methoxyphenyl)-1-propanol reacted with sodium hydrosulfide to form bis[1-(4-hydroxy-3-methoxyphenyl)-1-propyl] disulfide. At elevated temperatures complex reaction products were obtained. The product at 100° was slightly polymerized and contained 5.2% sulfur. At 160°, the sulfur compound was decomposed and additional polymerization took place. The product from the 160° cook contained 0.4% sulfur.

3. A similarity was noted in the reactivities of 1-(4-hydroxy-3-methoxyphenyl)-1-propanol and of native lignin with sodium hydrosulfide at room temperature. Native lignin was converted into a thiolignin containing 3.4% sulfur.

4. Carbonyl groups in the model compounds studied were extremely resistant to the action of the alkaline sulfide cooks. In the ordinary five-hour cooks at 160°, the carbonyl groups did not react to form sulfur derivatives. Even in an extended 30-hour cook at 160°, the carbonyl group of propiovanillone was not modified.

5. Although it is doubtful whether α, β-unsaturated ketones are present in significant amounts in lignin, a masked α, β-unsaturated group may be present. Therefore, the study of α, β-unsaturated ketones was carried out because such groupings may be formed in lignin during the kraft cook. In 2',4-dihydroxy-3-methoxychalcone, 4,4'-dihydroxy-3,3'-dimethoxychalcone, and 2-vanillylidene-3-coumaranone, the α, β-unsaturated ketone groups were almost completely hydrolyzed by a reverse aldol reaction during the cooks.

6. The sodium hydrosulfide cook of 4'-hydroxy-3'-methoxyflavanone was carried out to study the reactivity of a masked conjugated double bond. The products of the cook indicated that an initial reaction liberated the α, β-unsaturated ketone group. The successive reactions were the same as those that occurred in the 2',4-dihydroxy-3-methoxychalcone cook.

7. The action of the sodium hydrosulfide cook on the ether linkage was studied by cooking ω-(4-aceto-2-methoxyphenoxy)acetovanillone. The high yield of acetovanillone from the cook indicated that the ether linkage was cleaved by a reducing reaction.

8. Small amounts of demethylated products were isolated from all compounds except 1-(4-hydroxy-3-methoxyphenyl)-1-propanol. In cooking propiovanillone, demethylation was found to increase with an increase in cooking time. The model compounds exhibiting the demethylating reaction were similar in that all contained a carbonyl group adjacent to the benzene nucleus.

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